European Journal of Cardio-Thoracic Surgery 56 (2019) 230–270
doi:10.1093/ejcts/ezz098 Advance Access publication 17 May 2019

POSITION STATEMENT

Cite this article as: Potapov EV, Antonides C, Crespo-Leiro MG, Combes A, Färber G, Hannan MM *et al*. 2019 EACTS Expert Consensus on long-term mechanical circulatory support. Eur J Cardiothorac Surg 2019;56:230–70.

2019 EACTS Expert Consensus on long-term mechanical circulatory support

Evgenij V. Potapov[a,*†] (EACTS Chairperson), Christiaan Antonides[b,†], Maria G. Crespo-Leiro[c], Alain Combes[d,e], Gloria Färber[f], Margaret M. Hannan[g], Marian Kukucka[h], Nicolaas de Jonge[i], Antonio Loforte[j], Lars H. Lund[k], Paul Mohacsi[l], Michiel Morshuis[m], Ivan Netuka[n], Mustafa Özbaran[o], Federico Pappalardo[p], Anna Mara Scandroglio[q], Martin Schweiger[r], Steven Tsui[s], Daniel Zimpfer[t] and Finn Gustafsson[u,*] (EACTS Chairperson), The Task Force on Long-Term Mechanical Circulatory Support of the EACTS

[a] Department of Cardiothoracic and Vascular Surgery, German Heart Center Berlin, Germany; DZHK (German Centre for Cardiovascular Research), Partner Site Berlin, Germany
[b] Department of Cardiothoracic Surgery, Erasmus University Medical Center, Rotterdam, Netherlands
[c] Complexo Hospitalario Universitario A Coruña (CHUAC), Instituto de Investigación Biomédica de A Coruña (INIBIC), CIBERCV, UDC, La Coruña, Spain
[d] Sorbonne Université, INSERM, Institute of Cardiometabolism and Nutrition, Paris, France
[e] Service de médecine intensive-réanimation, Institut de Cardiologie, APHP, Hôpital Pitié–Salpêtrière, Paris, France
[f] Department of Cardiothoracic Surgery, Jena University Hospital, Friedrich-Schiller-University of Jena, Jena, Germany
[g] Department of Medical Microbiology, University College of Dublin, Dublin, Ireland
[h] Department of Anaesthesiology, German Heart Center Berlin, Berlin, Germany
[i] Department of Cardiology, University Medical Center Utrecht, Utrecht, Netherlands
[j] Department of Cardiothoracic, S. Orsola Hospital, Transplantation and Vascular Surgery, University of Bologna, Bologna, Italy
[k] Department of Medicine Karolinska Institute, Heart and Vascular Theme, Karolinska University Hospital, Solna, Sweden
[l] Department of Cardiovascular Surgery Swiss Cardiovascular Center, Inselspital, Bern University Hospital, Bern, Switzerland
[m] Clinic for Thoracic and Cardiovascular Surgery, Herz- und Diabeteszentrum Nordrhein-Westfalen, Bad Oeynhausen, Germany
[n] Institute for Clinical and Experimental Medicine (IKEM), Prague, Czech Republic
[o] Department of Cardiovascular Surgery, Ege University, Izmir, Turkey
[p] Advanced Heart Failure and Mechanical Circulatory Support Program, Cardiac Intensive Care, San Raffaele Hospital, Vita Salute University, Milan, Italy
[q] Department of Anesthesia and Intensive Care, San Raffaele Hospital, Vita Salute University, Milan, Italy
[r] Department of Congenital Pediatric Surgery, Zurich Children's Hospital, Zurich, Switzerland
[s] Royal Papworth Hospital, Cambridge, United Kingdom
[t] Department of Surgery, Division of Cardiac Surgery, Medical University of Vienna, Vienna, Austria
[u] Department of Cardiology, Rigshospitalet, Copenhagen, Denmark

* Corresponding authors. Department of Cardiothoracic Surgery, German Heart Centre Berlin, Berlin, Germany. Tel: 49-30-4593 2065; e-mail: potapov@dhzb.de (E.V. Potapov); Department of Cardiology, Rigshospitalet, 9 Blegdamsvej, 2100 Copenhagen, Denmark. Tel: +45-35-459743; e-mail: finng@dadlnet.dk (F. Gustafsson).

Abstract

Long-term mechanical circulatory support (LT-MCS) is an important treatment modality for patients with severe heart failure. Different devices are available, and many—sometimes contradictory—observations regarding patient selection, surgical techniques, perioperative management and follow-up have been published. With the growing expertise in this field, the European Association for Cardio-Thoracic Surgery (EACTS) recognized a need for a structured multidisciplinary consensus about the approach to patients with LT-MCS. However, the evidence published so far is insufficient to allow for generation of meaningful guidelines complying with EACTS requirements. Instead, the EACTS presents an expert opinion in the LT-MCS field. This expert opinion addresses patient evaluation and preoperative optimization as well as management of cardiac and non-cardiac comorbidities. Further, extensive operative implantation techniques are summarized and evaluated by leading experts, depending on both patient characteristics and device selection. The faculty recognized that postoperative management is multidisciplinary and includes aspects of intensive care unit stay, rehabilitation, ambulatory care, myocardial recovery and end-of-life care and mirrored this fact in this paper. Additionally, the opinions of experts on diagnosis and management of adverse events including bleeding, cerebrovascular accidents and device malfunction are presented. In this expert consensus, the evidence for the complete management from patient selection to end-of-life care is carefully reviewed with the aim of guiding clinicians in optimizing management of patients considered for or supported by an LT-MCS device.

Keywords: Mechanical circulatory support • Left ventricular assist devices • Heart failure • Expert consensus

† The first two authors contributed equally to this study.

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1. ABBREVIATIONS AND ACRONYMS

AR	Aortic regurgitation
BiVAD	Biventricular assist device
BSI	Bloodstream infection
CC	Cardiac cachexia
CF	Continuous-flow
CHD	Congenital heart disease
CPB	Cardiopulmonary bypass
EACTS	European Association for Cardio-Thoracic Surgery
EOL	End of life
EUROMACS	European Registry for Patients with Mechanical Circulatory Support
GI	Gastrointestinal
HF	Heart failure
HTx	Heart transplant
ICD	Implantable cardioverter defibrillator
iNO	Inhaled nitric oxide
INTERMACS	Interagency Registry for Mechanically Assisted Circulatory Support
INR	International normalized ratio
LT-MCS	Long-term mechanical circulatory support
LV	Left ventricle
LVAD	Left ventricular assist device
MCS	Mechanical circulatory support
PC	Palliative care
PVR	Pulmonary vascular resistance
RD	Renal dysfunction
RM	Remote monitoring
RV	Right ventricle
RVAD	Right ventricular assist device
TAH	Total artificial heart
TOE	Transoesophageal echocardiography
VA	Ventricular arrhythmia
VAD	Ventricular assist device

2. INTRODUCTION

Long-term durable mechanical circulatory support (LT-MCS) has evolved significantly in the last decade. Today's devices have become more reliable, and their durability has increased whereas device-related complications have drastically decreased compared with earlier generations of devices. In addition to a growing population with end-stage heart failure (HF), these developments have led to a notable increase in MCS implants, particularly of continuous-flow left ventricular assist devices (CF-LVADs). In Germany only, nearly 1000 LVADs were implanted in 2016 [1]. Thus, LT-MCS has become a standard of care in the treatment of end-stage HF. Moreover, the availability of smaller blood pumps together with growing clinical experience has expanded the target population by extending LT-MCS to patients with more complex conditions, including elderly and paediatric patients, patients with congenital heart defects and patients with advanced comorbidities. This expansion has resulted in a significant increase in the complexity of all aspects of management of these patients from selection to postoperative management, which is recognized in the presented consensus statement.

The European Association for Cardio-Thoracic Surgery (EACTS) has not recently provided guidance on LT-MCS. However, since the available scientific evidence consists mainly of observational studies with a few randomized clinical trials, it would not be feasible to formulate a full set of guidelines that meets EACTS criteria. Therefore, the EACTS provides an expert consensus statement in this document.

In this statement, we have generally refrained from using the designations of bridge to transplant and destination therapy in accordance with the more recent randomized trials in this field [2a]. This decision relates to the fact that, although a cardiac transplant is intended in the majority of LT-MCS recipients, only a minority will ever receive a donor organ in Europe. In a recent report of the ELEVATE (Evaluating the HeartMate 3 with Full MagLev Technology in a Post-Market Approval Setting) registry of more than 450 consecutive patients (mainly European) undergoing implantation of LT-MCS, only 2% received a transplant after 1 year, despite 26% of the patients receiving an implant as a destination therapy strategy [2b]. The latter also underscores the need for guidance of long-term management of MCS recipients, which consequently is an integral part of this statement.

As is stated in the present expert consensus, the multidisciplinary team of surgeons, intensive care specialists, cardiologists, perfusionists, LT-MCS coordinators, psychologists and other allied health care professionals should be involved in all stages of treatment of patients with LT-MCS. This goal is evident in the present expert consensus, which includes authors drawn from all the different specialties involved in the care of the patients with MCS. Furthermore, the chapters focusing on surgical aspects are complemented by chapters on medical management including patient selection, preoperative optimization, intensive care, ambulatory care and, finally, palliative care (PC).

3. METHODS

A task force of experts from cardiac surgery, cardiology, cardiac anaesthesiology and intensive care was assembled by the EACTS to formulate this expert consensus. The topic for the consensus was decided by the EACTS leadership. The task force members met to discuss all recommendations in a plenary session and utilized standard recommendation and evidence level nomenclature as described below (Tables 1 and 2).

Table 1: Classes of recommendations

Classes of recommendations	Definition	Suggested wording to use
Class I	Evidence and/or general agreement that a given treatment or procedure is beneficial, useful, effective.	Is recommended/is indicated
Class II	Conflicting evidence and/or a divergence of opinion about the usefulness/efficacy of the given treatment or procedure.	
Class IIa	*Weight of evidence/opinion is in favour of usefulness/efficacy.*	Should be considered
Class IIb	*Usefulness/efficacy is less well established by evidence/opinion.*	May be considered
Class III	Evidence or general agreement that the given treatment or procedure is not useful/effective, and in some cases may be harmful.	Is not recommended

Table 2: Levels of evidence

Level of evidence A	Data derived from multiple randomized clinical trials or meta-analyses.
Level of evidence B	Data derived from a single randomized clinical trial or large non-randomized studies.
Level of evidence C	Consensus of opinion of the experts and/or small studies, retrospective studies, registries.

A literature search was performed by the authors of the various chapters and an overall complementary literature search was performed by a member of the task force (C.A.).

4. PATIENT EVALUATION AND TIMING OF IMPLANTATION

4.1 Background

Patient evaluation and selection for LT-MCS as a therapy for advanced HF involves consideration of multiple factors. LT-MCS is associated with early and late risks of adverse events [3], substantial resource utilization and costs [4, 5], hospital readmissions [6] and the potential for considerable suffering for patients and families [7]. It is therefore crucial that patient selection achieves the greatest treatment effect possible by targeting patients with the highest benefit/risk ratio [8]. Current HF guidelines of the European Society of Cardiology [9] recommend the use of LT-MCS; however, selection criteria for evaluation of potential candidates are lacking. Nonetheless, extensive data are available that predict outcomes with and in the absence of LT-MCS.

4.2 Evidence review

Major trials have established the efficacy of LVADs in patients with a low left ventricular ejection fraction (≤25%), who were inotrope dependent or were persistently New York Heart Association (NYHA) functional class IIIb or IV despite optimal medical therapy. Additionally, a maximal oxygen consumption below 12 ml/kg/min was often used as an inclusion criterion.

4.3 Levels of the Interagency Registry for Mechanically Assisted Circulatory Support

The Interagency Registry for Mechanically Assisted Circulatory Support (INTERMACS) and the European Registry for Patients with Mechanical Circulatory Support (EUROMACS) stratify patients with advanced HF into 7 levels that are useful for guiding patient evaluation (Supplementary Material, Table S1) [10]. A majority of patients included in LT-MCS trials had INTERMACS levels 1–4. Outcomes with LT-MCS in INTERMACS level 1 are poorer than those in levels 2–3 and bridging with temporary MCS in the former is recommended [11, 12].

4.4 Biventricular failure

Patients with chronic biventricular failure with severe right ventricular failure are not good candidates for LT-MCS with LVAD therapy alone. Biventricular support with 2 blood pumps (implantable or extracorporeal) or implantation of a total artificial heart (TAH) should be considered. However, patients presenting with acute biventricular failure could initially be treated with a biventricular assist device (BiVAD) and may ultimately prove to be candidates for LVAD support only after a period of right ventricle (RV) unloading with a temporary right ventricular assist device (RVAD).

Due to the limitations of any single criterion to predict HF prognosis and MCS postoperative mortality, comprehensive risk assessment by a dedicated advanced HF team is recommended. Numerous single risk markers and composite risk scores have been derived and validated and are available as interactive online tools that can assist the heart team with comprehensive risk assessments and facilitate informed decisions (Supplementary Material, Table S2) [13–16]. However, most of the prognostic tools were derived and validated in clinical trial populations or from single-centre experiences. Therefore, these may not be generalizable to the 'real-world' HF population.

Nevertheless, objective risk markers and scores, if deployed as part of a comprehensive assessment by an HF team, are useful for prognostication and prioritization [17]. Clinical history such as recurrent HF hospitalizations and the physician's gestalt from the patient encounter are critical. Moreover, numerous plasma biomarkers of neurohormonal activation, cardiomyocyte injury or

stress, inflammation, fibrosis and multifactorial markers are independent markers of outcome in patients with advanced HF [18]. The cardiopulmonary exercise test provides a set of integrated parameters that represent not only cardiac but also peripheral function. This finding may be particularly helpful in selecting patients who are not inotrope-dependent for LT-MCS therapy, given the fact that impaired exercise tolerance was an inclusion criterion in most LT-MCS studies.

It is crucial to perform a thorough evaluation of the psychosocial situation of potential candidates for LT-MCS. For example, outcomes after LT-MCS implantation are inferior in patients living alone [19]. Active substance abuse is a contraindication to implantation of LT-MCS. Finally, non-patient-related factors, such as organization of care and access to follow-up and treatment, are also strongly associated with outcomes [20].

Recommendations for evaluation and selection of patients for LT-MCS therapy

Recommendation	Class	Level	References
It is recommended that reversible causes of heart failure are ruled out.	I	B	
LT-MCS implantation should be considered in patients with the following: • New York Heart Association functional class IIIB–IV and • Ejection fraction ≤25% and At least one of the following criteria: ○ INTERMACS 2–4 ○ Inotrope dependence ○ Progressive end-organ dysfunction ○ Peak VO_2 <12 ml/kg/min ○ Temporary MCS dependence	IIa	B	
LT-MCS implantation may be considered in patients with: • New York Heart Association functional class IIIB–IV and • Ejection fraction ≤25% and ○ To reverse elevated pulmonary vascular resistance or potentially reversible renal failure in potential heart transplant candidates ○ To allow time for transplant contraindications to be reversed such as recent cancer, obesity and recovering drug and alcohol dependence in potential heart transplant candidates	IIb	B	
Patient characteristics associated with a high risk of poor outcome post-left ventricular assist device			
LT-MCS in patients with advanced age, after careful evaluation of comorbidities and frailty, should be considered.	IIa	C	[3, 22–25]
LT-MCS in patients with peripheral vascular disease, depending on its severity, may be considered.	IIb	C	
LT-MCS in patients with active systemic bacterial/fungal infection is not recommended.	III	B	[26, 27]
In patients with well controlled HIV, hepatitis B or hepatitis C, LT-MCS should be considered.	IIa	B	[26, 27]
In patients with diabetes with poor glycaemic control or end-organ complications, LT-MCS may still be considered.	IIb	B	[22, 28–30]
LT-MCS may be considered in patients with chronic dialysis.	IIb	C	[31–34]
LT-MCS implantation in patients with haemostatic deficiencies and coagulopathies may be considered.	IIb	B	[35–38]
LT-MCS implantation in patients with untreated aortic regurgitation or mechanical aortic valve is not recommended.	III	C	[39, 40]
LT-MCS in patients with untreated severe mitral stenosis is not recommended.	III	C	
LT-MCS implantation in patients with irreversible liver dysfunction, as diagnosed by liver enzyme laboratory tests and the Model of End-stage Liver Disease score, is generally not recommended.	III	B	[41]
In patients with poor neurological and cognitive function, LT-MCS implantation is not recommended.	III	B	[42, 43]
Frail patients and patients with limited mobility may, after careful evaluation, be considered for LT-MCS implantation.	IIb	B	[44–48]
LT-MCS in patients who are living alone or who are suffering from depression should, after careful evaluation, be considered.	IIa	C	[19, 49–53]
LT-MCS implantation in patients who suffer from dementia is not recommended.	III	C	[19, 49–53]
LT-MCS implantation in patients with active substance abuse, not willing to cease the abuse, is not recommended.	III	C	
LT-MCS implantation in patients with malignancies may be considered if expected survival is >1 year.	IIb	C	[33]

HIV: human immunodeficiency virus; INTERMACS: Interagency Registry for Mechanically Assisted Circulatory Support; LT-MCS: long-term mechanical circulatory support.

Despite the availability of an extensive set of prognostic parameters, predicting outcomes both in the absence and presence of advanced HF interventions remains difficult. Furthermore, patients are often referred to specialized advanced HF centres too late. The concept of active screening for advanced intervention has been proposed to improve appropriate referral and treatment in patients with advanced HF [21].

5. PREOPERATIVE ORGAN FUNCTION OPTIMIZATION

In the context of HF, end-organ dysfunction is a hallmark of very advanced disease and is associated with increased risk of early death. Prior to surgery, a comprehensive patient evaluation to identify pre-existing comorbid conditions that may influence postoperative survival that could be optimized preoperatively is recommended [33].

Optimization plays a fundamental role in patients with INTERMACS levels 3–4 because there is more time for planning the implant [54, 55]. Preoperative optimization is in continuous interplay with haemodynamics, because low cardiac output and RV failure or fluid overload are key targets of treatment. In these perspectives, their potential for improvement and timing are pivotal. Indeed, the interaction between the RV and end-organ function is to be acknowledged because the latter is a risk factor for RV failure. At baseline, organ function should be routinely assessed with standard parameters; therefore, haemodynamic evaluation and the potential for its management with a tailored pharmacological or short-term MCS device should follow. Optimization does not mean normalization; a positive trend following specific treatment is to be taken as a goal. Similarly, no conclusion about reversibility of organ dysfunction can be drawn until cardiac output and filling pressures have been optimized. As a general rule, recent onset HF and young age may be associated with a higher probability of recovery of end-organ dysfunction if cardiac output is restored.

Recommendations for preoperative organ function optimization

Recommendation	Class	Level	References
Renal function			
In patients with renal dysfunction, optimization via improvement of cardiac output and reduction of filling pressures is recommended.	I	B	[56]
Liver function			
Liver function evaluation with bilirubin is recommended.	I	B	[57, 58]
In patients with increasingly elevated bilirubin levels, temporary MCS, ahead of possible LT-MCS implantation, may be considered.	IIb	B	[59]
Pulmonary function			
Treatment of preimplant pulmonary oedema is recommended before implantation.	I	B	[60, 61]
Left ventricular unloading on extracorporeal life support to optimize lung function should be considered.	IIa	B	[62]
Respiratory physiotherapy should be considered.	IIa	C	
Coagulation			
Withdrawal of dual antiplatelet therapy and/or vitamin K antagonists to reduce the risk of bleeding is recommended.	I	B	[63, 64]
The use of short-acting intravenous anticoagulation as bridging is recommended.	I	B	[64]
Administration of procoagulants shortly before implantation of the LT-MCS may be considered.	IIb	B	[64]
Optimization of coagulation prior to surgery should be considered, especially in patients on temporary MCS.	IIa	C	
Nutritional, metabolic and endocrine considerations			
Preoperative assessment of metabolic, endocrine and nutritional status, including possible interventions for arising issues, should be considered.	IIa	C	
Nutritional support, if necessary, may be considered.	IIb	C	[65, 66]

LT-MCS: long-term mechanical circulatory support.

6. CONCOMITANT CARDIAC CONDITIONS INCLUDING ARRHYTHMIAS

6.1 Background

To increase survival and to reduce the complication rates after the operation, preoperative evaluation and identification of other cardiac conditions are of utmost importance. Presence of concomitant cardiac diseases requires appropriate intraoperative planning [33, 67]. Although it is clear that mechanical valves in the aortic position must be replaced by a bioprosthetic valve prior to implantation of an LVAD or BiVAD, there is accumulating experience with leaving mechanical mitral valves *in situ*. Clearly, more data in this area are needed before firm recommendations regarding the requirement to replace the mechanical mitral valve can be made.

Recommendations for concomitant cardiac condition including arrhythmias

Recommendation	Class	Level	References
Aortic valve and root diseases			
Biological valve replacement in patients with more than mild aortic insufficiency should be considered.	IIa	B	[68, 69]
Application of a central leaflet coaptation stitch may be considered in patients with more than mild aortic insufficiency.	IIb	B	[68–70]
Closure of aortic valve in patients with more than mild aortic insufficiency is not recommended.	III	C	[68, 69]
It is recommended that a functional bioprosthesis be left in place.	I	C	[69, 71]
Replacement of a mechanical aortic valve with a biological valve is recommended.	I	C	[69, 71]
Closure of mechanical aortic valves is not recommended.	III	C	[68, 69]
Surgical correction of an ascending aorta aneurysm at the time of implantation of a ventricular assist device should be considered.	IIa	C	[70]
Mitral valve disease			
Correction of moderate or severe mitral stenosis of any cause (including transcatheter interventions) is recommended.	I	C	[71, 72]
In selected patients, the repair of severe mitral insufficiency may be considered.	IIb	C	[73–75]
Exchange of a functional mitral mechanical or biological prosthesis at the time of long-term mechanical circulatory support device implantation is not recommended.	III	C	[71]
In patients previously treated with a MitraClip, a thorough evaluation to rule out the existence of mitral valve stenosis is recommended.	I	C	
Tricuspid valve disease and right ventricular dysfunction			
Correction of severe tricuspid stenosis at the time of long-term mechanical circulatory support implantation is recommended.	I	C	
Re-evaluation of patients with moderate to severe tricuspid regurgitation after treatment with diuretic therapy, if condition permits, is recommended.	I	C	[76]
In carefully selected patients, tricuspid valve repair for moderate to severe tricuspid regurgitation at the time of long-term mechanical circulatory support implantation may be considered.	IIb	C	[77–80]
Implantation of a biventricular assist device or a total artificial heart in patients with severe tricuspid regurgitation and right ventricular dysfunction may be considered.	IIb	C	[81]
Intracardiac shunts			
Closure of a patent foramen ovale, either percutaneously or at the time of LT-MCS implantation, is recommended.	I	C	[71]
Depending on the shunt volume, closure of an iatrogenic atrial septal defect after trans-septal intervention is recommended.	I	C	
Intensive use of transoesophageal echocardiography in the operating room directly after LT-MCS implantation is recommended.	I	C	[71, 72]
Closure of a ventricular septal defect during LT-MCS implantation is recommended.	I	C	
In patients with an unrepairable ventricular septal defect, LT-MCS implantation is not recommended.	III	C	[71]

Continued

Recommendations for concomitant cardiac condition including arrhythmias *(Continued)*

Arrhythmia			
Medical or surgical intervention (according to European Society of Cardiology/European Heart Rhythm Association, Heart Rhythm Society Guidelines) for atrial tachyarrhythmia is recommended.	I	C	[79, 82, 83]
Routine implantation of an implantable ICD for primary prophylaxis before long-term mechanical circulatory support implantation is not recommended.	III	C	[84]
In patients with an ICD, preoperative evaluation of a possible ventricular assist device–ICD interaction may be considered.	IIb	C	[85]
Concomitant VT ablation during long-term mechanical circulatory support device implantation in patients with a history of frequent VTs may be considered.	IIb	C	[86, 87]
In patients with refractory, recurrent VT/ventricular fibrillation in the presence of an untreatable arrhythmogenic substrate (e.g. giant cell myocarditis or sarcoidosis), implantation of a biventricular assist device or a total artificial heart should be considered.	IIa	C	
Intracardiac thrombus			
Echocardiography, computed tomography or magnetic resonance imaging in patients suspected of having an intracardiac thrombus is recommended.	I	C	[71]
In patients with atrial fibrillation, due to the increased risk of thromboembolism from the LAA, a transoesophageal echocardiogram should be considered.	IIa	C	[72]
In patients with atrial fibrillation, LAA closure may be considered.	IIb	C	[88]
If a left atrial or ventricular thrombus is present, inspection and removal of the thrombus are recommended.	I	C	
If an LAA thrombus is present, occlusion of the LAA should be considered.	IIa	C	
Although RV and RA thrombi are less common, cardiac imaging to exclude them, in particular before implantation of an RVAD, should be considered.	IIa	C	[71]
In case of implantation of a left ventricular assist device, removal of an RV thrombus may be considered.	IIb	C	
In case of RVAD implantation in the RA, removal of an RV thrombus may be considered.	IIb	C	
In case of RVAD implantation in the RA, removal of an RA thrombus is recommended.	I	C	
In case of RVAD implantation in the RV, removal of an RV thrombus is recommended.	I	C	
Miscellaneous conditions			
A left thoracotomy approach may be considered in patients who have had prior cardiac surgery.	IIb	C	[89]
LT-MCS implantation in patients who have active infective endocarditis is not recommended.	III	C	[33]
Postponement of an LT-MCS implant may considered in patients who have had a recent myocardial infarction affecting the left ventricular apex if the situation allows.	IIb	C	[90]
Surgical or interventional revascularization at the time of LT-MCS implantation may be considered in patients with right ventricular ischaemia.	IIb	C	

ICD: implantable cardioverter defibrillator; LAA: left atrial appendage; LT-MCS: long-term mechanical circulatory support; RA: right atrium; RV: right ventricle; RVAD: right ventricular assist device; VT: ventricular tachycardia.

7. MANAGEMENT OF NON-CARDIAC COMORBIDITIES

7.1 Background

At the time of LT-MCS implantation, patients are usually in their mid-50s (EUROMACS: mean 51.7, median 55 years) [91] or older (International Society for Heart and Lung Transplantation Mechanically Assisted Circulatory Support Registry, second report: 72% at >50 years) [92]. The majority of candidates for LT-MCS are INTERMACS level 3 or less, meaning at least they are inotrope dependent. Advanced age and inotrope dependency are both associated with comorbidities. Therefore, a thorough preimplant examination is crucial to identify absolute contraindications for LT-MCS implantation such as surgical contraindications, severe coagulation and haematological disorders and irreversible multi-organ failure. Moreover, life-limiting comorbidities and the chance of improvement after LT-MCS implantation can be assessed.

7.2 Evidence review

Malignancies are often the reason to choose a bridge-to-candidacy strategy [93].

Frailty is a biological syndrome of impaired physiological and homeostatic reserve and heightened vulnerability to stressors, resulting from multiple morbidities, ageing and disability [94], occurring in nearly 10% of the patients in the INTERMACS Registry [95]. Frailty contains at least one of the following phenotype symptoms: shrinking, weakness, exhaustion, slowness and inactivity. No

specific definition has been validated, with the exception of the Fried scale [94, 96]. Frailty leads to significantly longer duration of mechanical ventilation, length of stay and long-term mortality in patients with LT-MCS [47, 48, 95]. After LT-MCS implantation, regression of frailty may occur [97]. Advanced age is a risk factor for frailty and comorbidities. However, several retrospective studies revealed acceptable outcomes after LT-MCS implantation in the elderly. Therefore, age alone should not be used as an exclusion criterion for LT-MCS implantation [98, 99].

Cardiac cachexia (CC) is the unintentional non-oedematous weight loss of >5% over at least 6 months. CC is associated with older age and can result in longer length of hospital stay and higher costs. CC (19%) is among the most common comorbidities of HF together with malignancies (34%) and chronic obstructive pulmonary disease (29%). Pathophysiological mechanisms of CC include metabolic and neurohormonal abnormalities [100]. However, the preoperative health status Kansas City Cardiomyopathy Questionnaire has limited association with outcomes after ventricular assist device (VAD) implantation [101]. For assessment of nutritional status, the prognostic nutritional index [serum (pre-) albumin and total lymphocyte count] might be used as an indicator of a worse outcome [102].

Renal dysfunction (RD) in advanced HF should be evaluated and categorized as primary or secondary dysfunction. LT-MCS implantation may reverse secondary RD [37, 56, 71, 103]. Severe RD (glomerular filtration rate <30 ml/min) increases the risk of the perioperative requirement for renal replacement therapy, early RV failure, infections and hospital mortality in patients with an LVAD [37, 56, 71, 103]. Primary RD should be ruled out. Primary non-reversible renal disease with severe RD may contraindicate LT-MCS implantation due to poor prognosis [37, 56, 71, 103]. Chronic haemodialysis should be considered as a relative contraindication for LT-MCS placement in highly selected patients. There are limited data on the safety of peritoneal dialysis while on LT-MCS support.

Preimplant major stroke is present in 3.6% of the patients in the INTERMACS Registry; other cerebrovascular diseases are present in 3.8%. Neurological and cognitive function should be assessed before LT-MCS implantation [104]. No worldwide accepted psychosocial assessment is available. The Stanford Integrated Psychosocial Assessment for Transplant can, however, certainly be used for LT-MCS candidates [105, 106].

Pre-LT-MCS evaluation of pulmonary function is mandatory [107]. There is a high prevalence of chronic obstructive pulmonary disease among patients with HF that can lead to a worse prognosis. Restrictive abnormalities and/or altered alveolo-capillary transfer may be a consequence of chronic pulmonary venous congestion. Re-evaluation after correction of fluid overload is recommended. To assess pulmonary hypertension, invasive haemodynamic assessment of pulmonary vascular resistance (PVR) is mandatory. Normalization of high PVR following LT-MCS support, thereby enabling a successful heart transplant (HTx), has been shown previously [108, 109].

Polysomnography is recommended in case of suspected sleep apnoea, drowsiness, periodic breathing and desaturation episodes, although the role of non-invasive ventilation in central sleep apnoea syndrome has been questioned.

Non-thyroidal illness syndrome has low levels of plasma T3 and T4, increased levels of reverse-T3 and normal or slightly decreased levels of thyroid-stimulating hormone. Non-thyroidal illness syndrome is frequent in critically ill patients (prevalence of 18%) and has a negative prognostic role. The early postoperative finding of low T3 syndrome is associated with a higher mortality rate and complications [110, 111].

Diabetes is common in recipients of LT-MCS (43%) but, in contrast to results from a previous study [28], does not increase mortality or serious adverse event rates during LT-MCS support [112, 113]. In a retrospective analysis ($n = 244$), LT-MCS therapy was associated with improvement in diabetic control that was attributed to improvements in cardiac output and normalization of biochemical derangements [114]. More awareness of diabetic patients with advanced HF is necessary [115].

Faecal occult blood testing during evaluation of potential candidate for LT-MCS is recommended. In the CF-VAD population, gastrointestinal (GI) bleeding is common and is associated with the occurrence of angiodysplasia [116] and acquired von Willebrand syndrome [117].

Hepatic dysfunction may occur as hypoxic hepatitis [118] in patients with acute HF or more commonly as 'cardiohepatic syndrome' in the setting of congestive HF [119–121]. Liver dysfunction is a predictor of poor outcome in patients with advanced HF requiring LT-MCS [41]. However, the liver has outstanding regeneration potential, which may occur after LT-MCS implantation [59, 63, 122–126]. Preoperative liver dysfunction influences the levels of circulating coagulation proteins and affects postoperative blood product requirements [127].

Short- or long-term MCS may rescue patients with peripartum cardiomyopathy [128]. Successful delivery in a patient with LT-MCS has been described [129].

Recommendations for the management of non-cardiac comorbidities

Recommendation	Class	Level	References
Malignancies			
Evaluation for malignancies is recommended.	I	A	
In patients with a proven malignancy and an expected survival of <1 year, implantation of long-term mechanical circulatory support is not recommended.	III	C	
Pulmonary hypertension			
Invasive haemodynamic assessment of pulmonary vascular resistance is recommended.	I	C	[107]
In heart transplant candidates, normalization of elevated pulmonary vascular resistance in patients on long-term mechanical circulatory support should be considered.	IIa	B	[108, 109, 130, 131]
Cardiac cachexia			
Assessment of frailty and nutritional status using a frailty score and/or prognostic nutrition index prior to implantation of long-term mechanical circulatory support may be considered.	IIb	C	[48, 96]

Continued

Recommendations for the management of non-cardiac comorbidities *(Continued)*

Renal dysfunction			
Implantation of long-term mechanical circulatory support should be considered in case of reversible secondary renal dysfunction.	IIa	C	[37, 56, 71, 103]
Implantation of long-term mechanical circulatory support may be considered in patients on chronic haemodialysis.	IIb	C	[37, 56, 103]
Neurological function and disorders			
Careful neurological examination is recommended for all candidates for implantation of long-term mechanical circulatory support including assessment of dementia and mental status.	I	C	[104, 132]
Multidisciplinary evaluation of prognosis of survival and morbidity of patients with neuromuscular disorders is recommended.	I	C	[133]
Adherence (medical therapy, alcohol, tobacco, psychological, psychiatric and social derangement)			
Screening for psychological and psychiatric (including cognitive function) disorders and substance abuse is recommended.	I	C	[104]
It is recommended that adherence (tobacco, alcohol and substance abuse), psychosocial risks and familial support be evaluated.	I	C	[134]
In patients with frailty, psychiatric or neurological disorders, evaluation of their ability to operate the device is recommended.	I	C	
Vascular disease			
Screening for peripheral vascular disease is recommended.	I	C	[67]
Coagulation and haematological disorders			
Evaluation of all long-term mechanical circulatory support candidates for coagulopathies and hypercoagulable states (e.g. thrombophilia) is recommended.	I	C	[135]
In patients with thrombocytopenia after exposure to heparin, testing for heparin-induced thrombocytopenia should be considered.	IIa	C	[136]
Respiratory considerations			
Spirometry as part of the patient work-up should be considered.	IIa	C	[25, 37, 137]
Preoperative thoracic imaging should be considered as part of the overall risk/benefit evaluation.	IIa	C	[25, 37, 137]
Diabetes			
Screening for diabetes mellitus (including end-organ damage) before implant of long-term mechanical circulatory support is recommended. For patients with poorly controlled diabetes, consultation with a diabetologist is recommended.	I	C	
Implantation of long-term mechanical circulatory support in patients with diabetes with severe end-organ complications is not recommended.	III	C	
Gastrointestinal disorders			
Gastrointestinal bleeding in patients 50 years or older: faecal occult blood testing, gastroscopy and endoscopy should be considered.	IIa	C	[116, 117]
Pregnancy			
Contraception in women of childbearing age after implant of long-term mechanical circulatory support is recommended.	I	C	
Long-term mechanical circulatory support in the setting of pregnancy is a multidisciplinary challenge and may be considered.	IIb	C	[128, 129]

8. SYSTEM SELECTION

8.1 Background

Implantable CF-LVADs represent the most common form of LT-MCS device used. However, some situations require temporary or permanent biventricular support and outcomes of patients depend on the appropriate choice of MCS strategy.

8.2 Evidence review

Centrifugal versus axial-flow implantable left ventricular assist devices.

- The currently approved axial-flow and centrifugal LVADs provide safe and effective circulatory support in a population of patients with end-stage HF [138–150].
- Centrifugal LVADs may facilitate implantation and offer options for different surgical approaches and strategies [151–154].

Left ventricular assist device versus biventricular assist device: impact of right heart function.

- A combination of clinical, haemodynamic, echocardiographic and biochemical parameters might be useful to assess right heart function preoperatively and to predict the need for perioperative mechanical RV support (Supplementary Material, Table S3).
- Levosimendan prior to LVAD implantation might be used to reduce the risk of right ventricular failure, although evidence is limited [155, 156].
- Echocardiographic assessment of RV geometry, contractility and valvular function (Supplementary Material, Table S4) prior to VAD implantation can be useful to evaluate the need for RV support [157–161].
- Patients with adequate right heart function who only require LVAD support have better survival rates, lower adverse event rates and superior quality of life than patients requiring BiVAD or TAH support [147, 162–173].
- RV failure requiring RVAD support is the most important risk factor for early death in LVAD recipients [170, 174–178].
- Temporary RVAD support should be considered in all recipients of an implantable LVAD, even in case of low RV failure risk score (RVAD required in 6–28% of LVAD recipients) [147, 178].
- Delayed institution or rescue implantation of RV support further increases the risk of morbidity and mortality compared to early RVAD implantation [147, 168, 169, 171, 179].

8.3 Biventricular assist device

Several BiVAD configurations exist: paracorporeal pulsatile-flow BiVAD, an implantable LVAD coupled with a concurrent paracorporeal or percutaneous RVAD or two implantable CF-LVADs. These conficurations provide comparable outcomes [173]. The insertion of two implantable CF-LVADs as BiVAD configuration is predominatly performed at experienced centers. However, the application of a CF-LVAD as an implantable RVAD remains an off-label use.

8.4 Temporary right ventricular assist device

- A temporary RVAD can be used while awaiting recovery of the RV after LVAD implantation and can be substituted with long-term RVAD support if required [170, 180].
- A temporary RVAD can be implanted percutaneously [181, 182] or surgically through a less invasive or sternotomy approach [183–186].

8.5 Longer-term right ventricular assist device

- Implantable BiVAD (e.g. 2 CF-LVADs) support might be considered in patients at high risk of RV failure having bridge to transplant [81, 187–191].
- Off-label use of implantable axial-flow or centrifugal LVADs has been adopted as RVAD support in conjunction with implantable LVAD support as an alternative to extracorporeal BiVAD or TAH implantation [192–196].

8.6 Total artificial heart

- TAH implantation is an option in bridge-to-transplant patients with biventricular failure and provides results comparable to those of BiVAD support [187, 193, 197–202].
- TAH implantation may be considered in patients with anatomical or other conditions that are not well served with 2 implantable LVADs or extracorporeal BiVAD such as in patients with small/non-dilated ventricles or patients requiring significant concomitant repair, e.g. restrictive/hypertrophic cardiomyopathy, cardiac tumour [203–206], complex postinfarction ventricular septal defect [207, 208] and congenital heart disease (CHD) with end-stage HF [209, 210].
- TAH might have a lower stroke incidence compared to BiVAD, resulting in a trend towards better survival [193, 211].

Recommendations for LT-MCS system selection

Recommendation	Class	Level	References
For predicting right heart failure, the use of clinical, haemodynamic, echocardiographic and biochemical parameters should be considered.	IIa	C	[170–174]
In patients with severe chronic biventricular failure, a BiVAD or a TAH should be considered.	IIa	B	[81, 147, 162–178, 187–191, 200, 203–208, 212]
In patients with refractory right heart failure after implantation of an LVAD, early implantation of a temporary RVAD should be considered.	IIa	C	[147, 168, 169, 171, 179]
Early RVAD implantation in case of right heart failure to decrease morbidity and mortality should be considered.	IIa	C	[147, 168, 169, 171, 179, 186]
Implantable BiVAD support may be considered in patients at high risk of right ventricular failure.	IIb	C	[81, 187–191]
Two CF-LVADs as an implantable BiVAD may be considered.	IIb	B	[192–196, 212, 213]
A TAH may be indicated in patients with biventricular failure, restrictive cardiomyopathy, cardiac tumours or large ventricular septal defects.	IIb	C	[187, 193, 197–201]
In patients with anatomical or other clinical conditions that are not well served with an LVAD or BiVAD, implantation of a TAH may be considered.	IIb	C	[203–208]

BiVAD: biventricular assist device; CF: continuous-flow; LT-MCS: long-term mechanical circulatory support; LVAD: left ventricular assist device; RVAD: right ventricular assist device; TAH: total artificial heart.

9. ANAESTHETIC MANAGEMENT

The clinical status of patients requiring LT-MCS varies considerably, from well-compensated (with poor cardiac reserve) to cardiogenic shock. Therefore, perioperative anaesthetic management is challenging [214–216].

9.1 Monitoring

For central venous access, ultrasound guidance is preferred due to the high incidence of thrombosis caused by previous indwelling catheters or transvenous pacemaker leads [217–220]. Although the impact of a pulmonary artery catheter on outcome has not been demonstrated for cardiac surgery [221], in relation to MCS implantation, pulmonary artery catheters provide valuable information including mixed venous oxygen saturation, pulmonary arterial pressure and vascular resistance that can guide intraoperative therapy decisions [222–224]. Neuromonitoring with electroencephalography is aimed at avoiding anaesthesia awareness [225]; cerebral perfusion can be assessed by estimating tissue oxygen saturation using near infrared spectroscopy [226].

9.2 Anaesthetic drugs

For induction, the use of propofol is not recommended due to its depressing effect on myocardial contractility and systemic vascular resistance. Therefore, etomidate (0.2–0.3 mg/kg) or a combination of midazolam and sufentanil are the preferred induction agents because myocardial contractility and systemic vascular resistance are unaffected [227]. Analgesia could be provided by short-acting opioids such as fentanyl or sufentanil. Anaesthesia is maintained using continuous infusion of propofol and an opioid.

Mechanical ventilation should avoid hypoxia and hypercarbia, which could result in an increase of PVR [228]. Protective ventilation settings with tidal volumes of 6–8 ml/kg and appropriate positive end expiratory pressure reduce the risk of ventilator-associated lung injury [229].

Transoesophageal echocardiography (TOE) has become an essential diagnostic and monitoring tool during LT-MCS implantation [230, 231]. Preprocedural TOE may identify intracavitary thrombus: thrombus size, localization and mobility may affect the surgical strategy. Furthermore, patent foramen ovale, other atrial and ventricular septal defects can be identified. If evaluation is inconclusive, contrast can be added.

Aortic regurgitation (AR) decreases the efficiency of LT-MCS. Therefore, it is recommended to not only assess AR before surgery but also when the patient is on cardiopulmonary bypass (CPB). CPB mimics the haemodynamic situation of VAD support with similar pressure and flow in the ascending aorta. In this setting, a final decision on aortic valve surgery can be made for borderline cases. Furthermore, TOE provides valuable information about right ventricular function and the tricuspid valve and can affect (concomitant) surgery [232].

Intraprocedural imaging of the inflow and outflow cannulas of the device is mandatory [233, 234]. Furthermore, TOE can help determine pharmacological support and pump speed settings while the patient is weaned from CPB, with special attention to the intraventricular septum in the 4-chamber view. Bulging of the intraventricular septum to the left and excessive unloading of the left ventricle (LV) indicate either excessive LVAD speed or RV failure.

Patients at risk of RV failure may benefit from primary pharmacological support to increase myocardial contractility and to decrease PVR using a combination of epinephrine, milrinone and inhaled pulmonary vasodilators [e.g. inhaled nitric oxide (iNO) or/and iloprost]. Observational studies have demonstrated a beneficial effect of iNO therapy [235, 236]. However, iNO did not significantly reduce the incidence of RV failure in a multicentre randomized study [237]. Expert panels concluded that it is reasonable to consider using iNO during LVAD implantation [238, 239].

Recommendations for anaesthetic management during LT-MCS implantation

Recommendations	Class	Level	References
Monitoring			
The introduction of an arterial line in advance of anaesthesia induction is recommended.	I	C	[214–216]
Use of a central venous line is recommended.	I	C	[214–216]
A pulmonary artery catheter should be considered.	IIa	C	[222–224]
Neuromonitoring with electroencephalography may be considered.	IIb	C	[225]
Neuromonitoring with near infrared spectroscopy should be considered, especially in off-pump implantation.	IIa	C	[243]
Periprocedural transoesophageal echocardiography			
It is recommended that the following assessments be performed using periprocedural transoesophageal echocardiography: intracavitary thrombus identification, detection of patent foramen ovale and other intracardiac shunts, assessment of aortic regurgitation, right ventricle assessment, inflow cannula positioning and outflow cannula positioning.	I	C	[230]
Assessment of right ventricular failure			
Transoesophageal echocardiography guidance for weaning from CPB/extracorporeal life support is recommended.	IIa	C	
iNO, milrinone and phosphodiesterase type 5 inhibitors to lower pulmonary vascular resistance should be considered.	IIa	B	[236, 244–246]

CPB: cardiopulmonary bypass; iNO; inhaled nitric oxide; LT-MCS: long-term mechanical circulatory support.

Early criteria for postprocedural diagnosis of RV failure are cardiac output <2.0 l/min/m^2, mixed venous oxygen saturation <55% and mean arterial pressure <50 mmHg [237]. High inotropic requirements and RV dilatation with concomitant collapse of the LV are signs of RV failure and should prompt the addition of temporary MCS for the RV [186].

If CPB is used, the suggested heparin dose is 400 IU/kg with a target activated clotting time of >400 s. If the patient is on extracorporeal membrane oxygenation (ECMO) or the ECMO remains implanted for a period after LVAD implantation (e.g. for support of the RV), a dose of 100 IU/kg heparin and a target activated clotting time of 160–180 s is recommended. Similarly, off-pump LVAD implantation is usually performed under heparin 100 IU/kg. Thromboelastometry- and thromboelastography-guided therapy results in a significantly lower re-exploration rate [240, 241] and a decrease in the incidence of postoperative acute kidney injury [242].

After LT-MCS implantation, preload should be optimized to ensure adequate VAD flows. However, overloading of the RV must be avoided. Any volume therapy should also take into account the likely quantity of blood products required to restore the coagulation status. To titrate volume status, assessment with TOE and the central venous pressure are essential.

10. OPERATIVE TECHNIQUE

The operative technique is subject to device-specific features as well as to the individual surgeon and institutional preferences. These recommendations summarize common steps in the surgical approach. However, patient-specific conditions, clinical status and the need for concomitant procedures may necessitate alternative or additional steps.

Recommendations for operative technique

Recommendations	Class	Level	References
Use of circulatory assistance during implantation: implant strategy			
The use of cardiopulmonary bypass during implantation of a long-term mechanical circulatory support device should be considered.	IIa	C	[37, 138, 141, 145, 247]
In case of no necessary concomitant intracardiac procedure, implantation of LT-MCS on extracorporeal life support or off-pump implantation may be considered.	IIb	C	[248]
In off-pump mechanical circulatory support implantation, secured vascular access for bail-out cardiopulmonary bypass is recommended.	I	C	[249, 250]
Mechanical circulatory support site preparation			
For non-intrapericardial devices, creation of the pump pocket by left hemidiaphragm transection to accommodate the pump is recommended.	I	C	[37]
For intrapericardial devices, in case of pericardial pouch-device mismatch, incising the pericardium to allow pump placement in the left pleural cavity may be considered.	IIb	C	[247]
Implantable left vascular assist device–inflow cannula placement			
Inflow cannula placement into the left ventricle is recommended.	I	A	[37, 138]
The use of transoesophageal echocardiography to check the inflow cannula position is recommended.	I	C	[37]
Placement of the inflow cannula parallel to the septum is recommended.	I	B	[37]
Inflow cannula placement in the inferior left ventricular wall may be considered.	IIb	C	
Inflow cannula placement in the lateral left ventricular free wall is not recommended.	III	C	[37]
Apical cuff positioning			
Apical cuff affixing with the sew first and then core technique, without other intraventricular manipulation necessary, is recommended.	I	C	[37, 251]
Apical cuff affixing with the sew first and then core technique with interrupted pledgeted sutures or continuous suture should be considered.	IIa	C	[251, 252]
Apical cuff affixing with the core first and then sew technique is recommended if intraventricular procedures, e.g. thrombus removal, mitral valve repair, are necessary.	I	C	[37, 251]

Continued

Recommendations for operative technique *(Continued)*

In the setting of acute left ventricular myocardial infarction due to friable tissue, the sew first and then core technique with use of circular reinforcement strips and surgical glue may be considered.	IIb	C	[251]
Apical cuff affixing with the core first and then sew technique with interrupted pledgeted reverse sutures may be considered.	IIb	C	[251]
In the setting of hypertrophic or non-compaction cardiomyopathies, a partial intracavitary excision prior to the apical cuff affixing may be considered.	IIb	C	[253, 254]
In the setting of acute left ventricular myocardial infarction with friable tissue of the apex, the use of temporary mechanical circulatory support may be considered to defer a long-term mechanical circulatory support implant.	IIb	C	
Implantable left ventricular assist device: outflow graft			
Performing the outflow graft anastomosis on the ascending aorta is recommended.	I	C	[37, 247]
Performing the outflow graft-ascending aortic anastomosis at a 45° angle should be considered to reduce the risk of late aortic insufficiency.	IIa	C	[37, 247]
The use of surgical glue to secure the haemostasis of the graft-aorta anastomosis may be considered.	IIb	C	[37]
Using the longitudinal line marker on the outflow graft to avoid twisting is recommended.	I	C	[37]
Positioning the outflow graft along the inferior right ventricular surface and between the right atrium and pericardium to avoid crossing the right ventricular outflow tract should be considered.	IIa	C	
Positioning the outflow graft through the transverse sinus onto the posterolateral aspect of the ascending aorta may be considered.	IIb	C	[255]
Implantable left ventricular assist device: alternative implant strategy/left thoracotomy approach			
An intrapericardial course of the outflow graft in patients without previous cardiac surgical procedures is recommended.	I	C	[37, 247]
The outflow graft anastomosis to the descending aorta may be considered in redo patients and patients with a severely calcified ascending aorta.	IIb	C	[152–154, 256, 257]
A left pleural cavity course of the outflow graft in redo implants with the anastomosis on the ascending aorta may be considered.	IIb	C	
In redo implants or for patients in whom an aortic anastomosis is not amenable, anastomosis of the outflow graft to the axillary artery may be considered. In this scenario, distal banding of the axillary artery to avoid hyperperfusion may be considered.	IIb	C	[153, 258]
Driveline externalization			
The course of the driveline with an intermediate incision (C-shape) to maximize the pump-to-exit site distance and to alleviate traction forces may be considered.	IIb	C	[259]
A partial course of the driveline through the rectus abdominis muscle to enhance the barrier for infection is recommended.	I	C	[260]
It is recommended that the portion of the driveline covered in velour is completely intracorporeal.	I	C	[259, 260]
Air embolism prevention			
Carbon dioxide insufflation within the surgical field is recommended.	I	B	[261, 262]
Having the patient in the Trendelenburg position at the time of de-airing may be considered.	IIb	C	[37]
Liberal de-airing via the outflow graft is recommended with on-pump surgery.	I	C	[37]
Oversewing or glue application on the outflow graft de-airing spot to obviate late bleeding in patients having anticoagulation therapy may be considered.	IIb	C	
Careful de-airing strategy in off-pump implantation should be considered.	IIa	C	[263]
Active suction (needle venting) may be considered.	IIb	C	
Alternative implant surgical strategy			
Left anterior thoracotomy at a level of the apex validated by echocardiography or computed tomography is recommended.	I	C	[151–154]
A partial upper sternotomy for the outflow graft anastomosis may be considered.	IIb	C	[151, 152, 154]

Continued

Recommendations for operative technique *(Continued)*

A right lateral thoracotomy for the outflow graft anastomosis may be considered.	IIb	C	[151, 153]
An alternative implant strategy with the outflow graft tunnelled via pleural cavities in redo implants without the need for major concomitant procedures may be considered.	IIb	C	
In patients with a history of cardiac surgery through a median sternotomy and who do not require concomitant cardiac surgery other than implantation of long-term mechanical circulatory support, implantation through a left lateral thoracotomy with connection of the outflow graft to the descending aorta may be considered.	IIb	C	
Closing surgical operation field considerations			
Liberal use of chest and pleural drains is recommended.	I	C	[37]
In the case of major coagulopathy, a provisional chest closure with surgical packing may be considered.	IIb	C	[264]
In patients with the prospect of a heart transplant, strategies to limit adhesions during implantation should be considered.	IIa	C	
Biventricular support			
Use of temporary short-term right heart support to allow for a subsequent explant without sternal reopening should be considered. Various possibilities can be considered: cannulation of the right atrium via the femoral vein for blood inflow and for blood return cannulation of vascular graft attached to the pulmonary artery or cannulation through the jugular vein. An additional option may be an endovascular microaxial pump inserted into pulmonary artery.	IIa	C	[265]
For implantable right ventricular assist device support, insertion of the inflow cannula insertion into the right atrium should be considered.	IIa	C	[265, 266]
For implantable right ventricular assist device support, insertion of the inflow cannula into the right ventricle may be considered.	IIb	C	[266, 267]
Long-term paracorporeal support			
Apical cannulation of the left ventricle should be considered for the left side of the pump.	IIa	C	[188]
In patients with restrictive/obstructive cardiomyopathy, cannulation in the left atrium may be considered.	IIb	C	[268]
Total artificial heart			
An atrial connection at the level of the atrioventricular valves and outflow grafts connected to the great vessels are recommended.	I	C	[192, 193, 196, 206, 269, 270]
Long-term mechanical circulatory support explant			
Complete circulatory support system explant is recommended in cases of active device infection or in patients at a high risk of infective complications.	I	C	[271]
After mechanical circulatory support explant for infection, stabilization with temporary mechanical circulatory support in conjunction with comprehensive antimicrobial therapy may be considered as a bridge to reimplantation.	IIb	C	[263]
After myocardial recovery without signs of infection, removal of the pump with a dedicated titanium sintered plug, outflow graft ligation and removal of the driveline should be considered where possible.	IIa	C	[267, 272]
After heart recovery without signs of infection, decommissioning with outflow graft ligation or endovascular occlusion with partial removal/internalization of the driveline may be considered.	IIa	C	[273, 274]

LT-MCS: long-term mechanical circulatory support.

11. PAEDIATRIC OPERATIVE TECHNIQUES

11.1 Introduction

The success rate of bridging children with MCS to a transplant or recovery using pulsatile or CF devices has improved with time. In the latest PEDIMACS report, an 84% 6-month survival rate on devices was reported with a transplant rate of nearly 50% [275], whereas the first Paedi-EUROMACS report shows a 6-month survival of 81% and a transplant rate of more than 50% [276]. Paediatric data on intracorporeal devices from EUROMACS demonstrated an on-device survival rate of 89% at 12 months [277]. Originally, the MCS devices used were mainly paracorporeal devices. More recently, an increase in the use of CF-LVAD in paediatric patients and patients with CHD has been reported [275, 278–281]. The obvious advantage is the ability to discharge these young patients home [282–286].

11.2 Small children—system selection

Device selection in children and patients suffering from CHD (see section below) differs significantly from that in adults with anatomically normal hearts and also differs substantially among paediatric groups depending on age and the type of CHD of the patient [275, 287, 288]. The Berlin Heart EXCOR® Paediatric VAD is currently the only VAD specifically designed and approved for the paediatric population in the USA, Europe and Canada.

In paediatric patients with a body surface area >1.2 m^2 requiring MCS, the use of an implantable CF-LVAD is feasible because

results are non-inferior to those with extracorporeal devices [275, 289, 290], and discharge from the hospital is possible, resulting in a better quality of life [275, 277, 284, 285, 290]. In adults, CF-VADs have improved survival and greater freedom from stroke and device failure compared with pulsatile devices [147]. This result seems to be true also for paediatric patients with a body surface area >1.2 m^2 and without CHD [275, 277, 279, 290].

11.3 Single ventricle–Fontan haemodynamics

Approximately 5–10% of children born with CHD suffer from an underdeveloped LV or RV, leading to single ventricle physiology. Large studies on the use of MCS in patients with a single ventricle are lacking. Only case reports or small case series have been published, and they report high mortality rates [283, 291, 292]. However, implantation of VADs in various locations seems to be feasible.

The feasibility of VAD support for Glenn circulation has been reported with mixed results [283, 292, 293]. After the Fontan circulation has been created, there are 2 possibilities of failure: systemic ventricular failure or failure at the level of the cavopulmonary connection. Currently available VADs are designed to support the failing ventricle. Nevertheless, available devices have been used for cavopulmonary support in patients with failing Fontan circulation [294, 295]. Others use clinically available VADs as a bridge to transplant [296–299]. For patients with failing Fontan circulation, TAH might be a viable option [300]. In cases of failing Fontan circulation and ventricular failure, the BiVAD remains an option but requires revision of the Fontan pathway to allow the separation of the systemic venous and pulmonary circulations, which can be very demanding.

11.4 Total artificial heart

A certain percentage of patients require biventricular support with either BiVAD placement or implantation of a TAH. The 70-cc TAH (SynCardia Systems Inc., Tucson, AZ, USA) is currently the only Food and Drug Administration (FDA)-approved and *Conformité Européenne* (CE)-marked TAH licensed for bridge to transplant or destination therapy. However, this device is limited to patients with a larger chest cavity with adequate intrathoracic space to accommodate this device. The 50 cc-TAH (currently under investigation for FDA approval) is more appropriate for use in smaller patients, especially in complex cases who have had limited clinical options such as failing Fontan circulation [300]. Unsurprisingly, reported outcomes in patients ≤21 years supported with a TAH seem to be inferior to LVAD-only implantation [301].

11.5 Special cases

Besides the 'single ventricle physiologies', CHD includes a wide spectrum of cardiac anatomical configurations, including surgically corrected transposition of the great arteries using the atrial switch procedure (Senning or Mustard operation) at infancy/childhood or patients with corrected congenital transposition of the great arteries. VAD placement in these patients is possible, and some patients will benefit from VAD support [275, 302–307]. However, limited data make standardized recommendations impossible. Each case has to be discussed individually, preferably by a dedicated heart team. Adult CHD and non-adult CHD patients supported by LVADs demonstrate similar survival regardless of cardiac anatomy [275].

Recommendations for paediatric operative techniques

Recommendation	Class	Level	References
Device selection in small children			
Implantation of a device with patient-device size mismatch is not recommended.	III	C	
If mid- to long-term mechanical circulatory support is anticipated, durable implantable or extracorporeal devices should be considered over extracorporeal life support.	IIa	B	[308–310]
In children in need of mechanical circulatory support, implantation of an intracorporeal continuous-flow left ventricular assist device and subsequent discharge home should be considered.	IIa	C	[275, 277, 278, 284, 285, 289, 290, 311]
Use of a SynCardia total artificial heart			
In complex congenital heart disease, patients, especially those with biventricular failure, with an adequate chest cavity and/or adequate intrathoracic space, a TAH may be considered as a bridge to transplant or as destination therapy.	IIb	C	[301]
If a TAH placement is planned, a virtual fit/implantation is recommended.	I	C	[312–314]
Patients with congenital heart disease requiring mechanical circulatory support			
It is recommended to have recently obtained documentation of cardiac morphological and ventricular physiological data after the last surgery, including the presence of shunts, collateral vessels and the location and course of great vessels in patients with congenital heart disease undergoing evaluation for mechanical circulatory support implantation.	I	C	[71, 275, 315, 316]

TAH: total artificial heart.

12. POSTOPERATIVE MANAGEMENT IN THE INTENSIVE CARE UNIT

Successful outcomes after cardiac surgery for LT-MCS depend on optimum postoperative care in the intensive care unit. Key elements of this multifaceted bundle of care include appropriate monitoring, with specific attention to right ventricular function, optimized volume and inotropic support, adequate management of sedation, analgesia, and ventilation and appropriate anticoagulation and transfusion strategies. Patients supported with LT-MCS should have standard monitoring used in the institution for patients after cardiac surgery. Additional monitoring specific for these patients is presented below.

Recommendations for postoperative management in the intensive care unit

Recommendation	Class	Level	References
Monitoring			
In postoperative patients with mechanical circulatory support, continuous electrocardiography, pulse oximetry, central venous pressure and invasive arterial blood pressure monitoring are recommended.	I	C	
Miniaturized transoesophageal echocardiographic probes that can be maintained in the oesophagus *in situ* for up to 72 h may be considered to assist in the management of fluid resuscitation and to diagnose complications.	IIb	C	[317]
A pulmonary artery catheter should be considered to assist in the management of fluid resuscitation and to diagnose complications in patients receiving an LVAD and at risk of postoperative RV failure.	IIa	C	[71, 318]
Transpulmonary thermodilution and pulse contour-derived measurement of cardiac output are inadequate in continuous-flow ventricular assist device and biventricular assist device settings and are therefore not recommended.	III	C	
Postoperative laboratory monitoring, including daily measurement of plasma free haemoglobin and lactate dehydrogenase, is recommended.	I	C	
Right ventricular failure in patients with a left ventricular assist device			
Regular echocardiographic scans should be considered to monitor RV function in patients supported by an LVAD.	IIa	C	[317, 319, 320]
Echocardiography is recommended to guide weaning from temporary RV support.	I	B	[321, 322]
Inhaled NO, epoprostenol (or prostacyclin) and phosphodiesterase 5 inhibitors may be considered to reduce right heart failure after LVAD implantation.	IIb	C	[323–327]
Inotrope and vasopressor support			
Norepinephrine should be considered as a first-line vasopressor in case of postoperative hypotension or shock.	IIa	B	[9, 328, 329]
Dopamine may be considered in case of postoperative hypotension or shock.	IIb	B	[9, 328, 329]
The combination of norepinephrine and dobutamine should be considered instead of epinephrine in case of postoperative hypotension and low cardiac output syndrome with RV failure.	IIa	C	[9, 71, 330, 331]
Epinephrine may be considered in case of postoperative hypotension and low cardiac output syndrome with RV failure.	IIb	C	
Phosphodiesterase 3 inhibitors may be considered in patients with long-term mechanical circulatory support with postoperative low cardiac output syndrome and RV failure.	IIb	C	[332, 333]
The use of levosimendan in case of postoperative low cardiac output syndrome may be considered.	IIb	A	[334, 335]
Postoperative mechanical ventilation			
Avoidance of hypercarbia that increases pulmonary artery pressure and RV afterload is recommended.	I	C	
Bleeding and transfusion management			
If mediastinal drainage exceeds 150–200 ml/h in the early postoperative phase, surgical re-exploration should be considered.	IIa	C	
Activated recombinant factor VII may be considered as a salvage therapy for intractable haemorrhage after correction of bleeding risk factors and after exclusion of a surgically treatable cause of bleeding.	IIb	C	[336, 337]

LVAD: left ventricular assist device; NO: nitric oxide RV: right ventricular.

13. ANTICOAGULATION

13.1 Background

LT-MCS devices require antithrombotic therapy due to the presence of the artificial surfaces of the pump and the modified fluid dynamic pattern of the blood accompanied by shear forces. Anticoagulation for LT-MCS comprises 3 different periods: preoperative, intraoperative and early postoperative. Management is often similar to that of other cardiac surgery procedures [64]; however, some situations require specific considerations as outlined below. Each phase has distinct issues and requires specific management. Long-term antithrombotic therapy is more standardized, although patients may tread a fine line between bleeding and thrombosis. Furthermore, the optimal long-term regimen of anticoagulation should be tailored to the recipient and the device type. In this context, the development of clinical analysis tools and/or risk scores is encouraged.

13.2 Description of evidence

Preoperative conditions. Normalization of coagulation before LT-MCS implantation is crucial to avoid the postoperative cascade of bleeding, transfusions and volume overload, RV failure and surgical re-exploration. Preoperative temporary MCS, in

particular, requires an antithrombotic regimen with intravenous drugs. Coagulopathy is inevitably present due to activation and consumption of coagulation factors secondary to cardiogenic shock and exposure to biomaterials and devices. This condition requires specific and more aggressive preoperative treatment.

Intraoperative conditions. Intraoperative full anticoagulation is recommended and, in line with other cardiac surgery protocols, with full reversal and restoration of blood components and coagulation factors at the end [64], except for off-pump surgical techniques or implant of extracorporeal life support, where a lower dose of heparin may be considered.

Postoperative conditions. Postoperative early anticoagulation is mandatory to prevent thrombotic events. Intravenous administration is the primary choice: unfractionated heparin is commonly used, but successful use of direct thrombin inhibitors has been reported. Anticoagulation can be commenced 8 h after surgery with all devices if bleeding is <50 ml/h [338]. Initially, the target activated partial thromboplastin time is 40 s; it is progressively increased to 55–60 s within the first 48–72 h postoperatively. Oral anticoagulation with the vitamin K antagonist should be initiated once the clinical condition is considered stable and oral intake is possible. The international normalized ratio (INR) target is set according to device recommendations for modern LT-MCS devices. The INR target is between 2.0 and 3.0. Acetylsalicylic acid is routinely administered according to device specifications. The use of new oral anticoagulants is currently not recommended.

Measurement of both the activated partial thromboplastin time and factor Xa are recommended for monitoring anticoagulation therapy. Bridging with intravenous heparin is recommended if the INR is <2.0 and in cases of planned invasive procedures or non-cardiac surgical procedures for perioperative bridging. Low-molecular-weight heparin may be considered as well.

Frequent INR checks using home INR monitoring and dedicated staff (for instance, trained pharmacists) permit strict anticoagulation management [339, 340]. Intravenous direct thrombin inhibitors such as bivalirudin and argatroban should be used as alternative anticoagulation agents for patients with heparin-induced thrombocytopenia.

Antithrombotic therapy should be patient-tailored during the time on support and in the different clinical situations. Technical equipment necessary for in-depth analysis is not yet available for point-of-care testing [341], thus preventing a more detailed approach in routine clinical practice.

Recommendations for the use of anticoagulation during LT-MCS

Recommendations	Class	Level	References
Management of anticoagulation preoperative, perioperative and postoperative of LT-MCS implantation			
If intraoperative extracorporeal life support or off-pump implantation is performed, administration of a reduced dose of heparin may be considered.	IIb	C	
Early postoperative anticoagulation starting with intravenous anticoagulation, followed by vitamin K antagonists, is recommended.	I	C	
The use of low-molecular-weight heparin as an early postoperative anticoagulation regimen should be considered.	IIa	C	[341]
A postoperative international normalized ratio target between 2.0 and 3.0 is recommended.	I	C	
The use of acetylsalicylic acid is recommended.	I	C	
The use of low-molecular-weight heparin for bridging during long-term support is recommended.	I	C	
Re-evaluation of antithrombotic therapy during bleeding episodes is recommended.	I	C	
The use of novel oral anticoagulants is not recommended.	III	B	[342]
Management of anticoagulation in the event of bleeding episodes			
For a major bleeding event, discontinuation of anticoagulation and reversal with blood components and coagulation factors are recommended.	I	C	[343]
For minor bleeding, if the INR is above the therapeutic range, adjustment of anticoagulation agents should be considered.	IIa	C	
In all cases of bleeding, exploration and treatment of a bleeding site should be considered.	IIa	C	[344]
After resolution of the first bleeding episode, discontinuation of long-term acetylsalicylic acid should be considered.	IIa	C	

INR: international normalized ratio; LT-MCS: long-term mechanical circulatory support.

14. REHABILITATION

14.1 Background

LT-MCS devices are implanted in patients with end-stage HF who commonly present with severely impaired functional capacity. Despite the lack of generally accepted recommendations for patients with LT-MCS, evidence is gathering that cardiac rehabilitation is beneficial. The goal is to return an MCS-supported patient to a normal and independent life. Besides the typical goals of cardiac rehabilitation, which include improvements in functional capacity and motor strength, specific additional goals in patients with LT-MCS are to educate them to understand the operation and handling of the device, self-management of sub-therapeutic INR, driveline exit site care as well as psychological and social counselling. In addition to the index rehabilitation immediately after LT-MCS implantation, repeated rehabilitation can become necessary in patients who exhibit adverse events (e.g. neurological complications) or those presenting with extreme deconditioning.

14.2 Evidence review

All patients after LT-MCS implantation should undergo cardiac rehabilitation in a rehabilitation centre familiar with the special challenges of MCS [71, 345]. To achieve independence and mobility in daily life, a multimodal rehabilitation programme consisting of endurance and strength training should be combined with education on handling the device and peripherals as well as anticoagulation self-management. Patients with neurological complications after VAD implantation should undergo rehabilitation in a centre with combined cardiac and neurological rehabilitation facilities.

Exercise and strength training should be performed in accordance with the recommendations for patients with HF and has repeatedly been shown to be safe in patients with LT-MCS [346–348]. During the index rehabilitation, exercise training should be performed using bicycle ergometry to minimise the risk of falls or other accidents. Exercise training can be guided by the perceived level of exertion as measured by the modified Borg Scale and should be performed at a higher level (around 13), which accounts for training between the anaerobic threshold and the respiratory compensation point [348–350]. Alternatively, a baseline cardiopulmonary stress test can be used to guide exercise training. This approach has been shown to significantly improve peak VO_2 in several series of patients with LT-MCS from baseline values as low as 10 to >14 ml/kg/min at discharge [348, 350, 351]. Strength training should focus on the muscle groups of the lower extremities, which are important for mastering the activities of daily life (standing up, walking performance) and are also prone to early deconditioning in critical illness [352]. Specifically, leg press, leg extensor, leg flexor, lower limb abductors and adductors should be trained [352]. Similar to exercise training, the appropriate level of exertion can be determined using the modified Borg Scale [348, 351, 353]. Structured walks and other group activities can complement exercise and strength training. These should further be complemented by physiotherapy and occupational therapy that are tailored to the individual patient's needs.

Patients should be educated about the importance of fluid balance and treatment compliance. In addition, patients should be educated about home INR monitoring and INR self-management to promote independence after discharge (see Chapter 13).

Patients and caregivers should be educated about handling the assist device as well as the required actions to typical alarms.

Recommendations for rehabilitation after LT-MCS implantation

Recommendations	Class	Level	References
Cardiac rehabilitation is recommended for patients with long-term mechanical circulatory support.	I	B	[345, 347, 348]
Rehabilitation in a centre familiar with patients with long-term mechanical circulatory support is recommended.	I	C	[345]
Psychosocial rehabilitation should be considered.	IIa	C	
Rehabilitation including a combination of exercise and strength training is recommended.	I	C	[352]
Exercise training using a level of perceived exertion or cardiopulmonary stress testing should be considered.	IIa	C	[350]
Physiotherapy and occupational therapy, depending on the individual's needs, should be considered.	IIa	C	
Educating patients on international normalized ratio self-monitoring should be considered.	IIa	C	
It is recommended that patients and caregivers are educated about handling long-term mechanical circulatory support peripherals and required reactions to typical alarms.	I	C	

LT-MCS: long-term mechanical circulatory support.

15. OUTPATIENT CARE

15.1 Mechanical circulatory support programme organization

An LT-MCS programme requires organization, planning and appropriate personnel to constitute a core MCS team [25, 37, 71, 137, 284, 354–362]. Mid- and long-term success for outpatients on LT-MCS therapy depends on a multidisciplinary approach. Such success is achieved by combining the expertise of MCS coordinators, advanced HF cardiologists, cardiovascular surgeons and other health care providers.

15.2 Discharge after ventricular assist device implantation

Successful discharge planning begins preoperatively, with assessment of the cognitive abilities of the patients, their support

system and home environment [25, 37, 71, 137, 284, 354–360]. Training of patients, family and other designated caregivers should be performed in the implanting hospital by the LT-MCS team.

A clear algorithm for when and how to seek help, including a synoptic card placed in the pocket and in the room of the patient at home with emergency instructions and contacts, is mandatory [25, 37, 71, 137, 284, 354–360]. The MCS team is responsible for informing the general practitioner, the referring physician and the emergency support personnel of the discharge of the patient with MCS. Those involved with the patient should be provided with basic knowledge of the concepts of MCS.

It is recommended that discharged patients regularly visit the outpatient clinic. During each visit, the following procedures should be considered: physical examination with special attention for the driveline exit site and blood pressure (BP), laboratory testing (including coagulation and markers of haemolysis), technical examination of the device, chest radiogram and echocardiographic scans.

15.3 Driveline site management

Roughly half of the patients develop infection of the exit site [71, 259, 363–376], making visual inspection of the wound at every outpatient visit essential. Additionally, attention should be paid to proper driveline positioning and the use of immobilization devices. A photographic record and clinical scoring of the driveline exit site are helpful in tracking its appearance over time [71, 259, 363–376]. The incidence of infection after LT-MCS implantation depends on patient-related risk factors [71, 259, 363–376].

Strict attention to driveline cleanliness should be ensured from postoperative day 0 [363, 367, 369, 370, 374, 376]. Initially, the dressing should be changed once daily, thus keeping the exit site dry. The use of various anchoring devices to stabilize the driveline helps minimize the risk of trauma.

The patients should receive in-house training for driveline care with family members before hospital discharge [363, 367, 369, 370, 374, 376]. After discharge, patients and/or their caregivers should adhere to the proper aseptic technique. A driveline management pack for changing the dressing should be given to the patient. Dressings should be changed by patients and/or their family members and/or their caregivers 1–2 times per week according to the condition of the exit site and the opinion of the VAD coordinator. Since patients with LT-MCS are susceptible to infections, they should avoid situations that could place them at an increased risk [71, 259, 363–376].

15.4 Blood pressure management and heart failure medication

Many patients still suffer from volume overload after LT-MCS implantation [71, 377–384]. Therefore, most patients require diuretics after LVAD implantation. Diuretic doses must be reviewed regularly to ensure relief of fluid overload and to avoid depletion of intravascular volume, which could result in suction events, pump alarms, arrhythmias and syncope.

Hypertension leads to increased afterload for the LVAD, decreased LVAD flow and less effective left ventricular unloading [71, 377–384]. Furthermore, there is a significant association between Doppler-derived BP and a range of adverse events including intracranial haemorrhage, thromboembolic events and progressive aortic insufficiency [71, 377–385].

With CF-LVADs, conventional measurement of BP is difficult. Thus it is common practice to use a Doppler BP reading as the mean systemic BP [382]. Newer oscillometric devices show good correlation of systolic, diastolic and mean pressures in patients with a CF-LVAD in comparison with intra-arterial pressure [378].

As a therapy, angiotensin converting enzyme inhibitors or angiotensin receptor blockers are the first-line drugs for post-LT-MCS hypertension. Beta-blockers can be used in combination with angiotensin-converting enzyme inhibitors or angiotensin receptor blockers but caution should be exercised in patients with marginal RV function. These agents may also be useful for rate control in the setting of atrial or ventricular arrhythmias (VAs). Calcium antagonists, especially the dihydropyridines, can be used as a third option. Aldosterone antagonists should be used for their potassium-sparing and antifibrotic effects.

15.5 Driving while on long-term mechanical circulatory support

Every country has its own regulations with regards to driving with medical conditions, physician/provider responsibility in reporting these conditions and physician/provider liability for motor vehicle accidents that might occur as a result of these patients driving. According to the literature [386–391], most patients with an LT-MCS, NYHA functional class I–III and stable LT-MCS implantation qualify for private driving only and are disqualified from commercial driving. A recent study shows that a significant number of patients with LT-MCS continue to drive a vehicle after implantation (72%), although the frequency of driving dropped from nearly 80% driving daily to 52% [392].

15.6 Remote monitoring

Remote monitoring (RM) can aid in outpatient care and surveillance of key parameters [71, 359–362]. RM provides a real-time view and transmission of MCS data via secure wireless Internet-based RM settings, thus potentially avoiding unnecessary hospital visits. The use of RM technology has only recently become available for some LT-MCS systems. Future developments may ease troubleshooting, provide more data from the patient and the pump and eventually increase physician and patient satisfaction.

Recommendations for outpatient care

Recommendation	Class	Level	References
Mechanical circulatory support programme management			
Management of outpatients with mechanical circulatory support therapy by a dedicated and specialized multidisciplinary team is recommended.	I	B	[25, 37, 71, 137, 284, 354–360]
Successfully discharging a patient with mechanical circulatory support			
Patient and caregiver education/training regarding device management, anticoagulation monitoring and driveline care is recommended.	I	B	[25, 37, 71, 137, 284, 354–360]
Blood pressure management			
In patients with continuous-flow mechanical circulatory support, a mean systemic blood pressure goal of ≤85 mmHg is recommended.	I	B	[71, 377–384]
Driveline dressing management			
It is recommended that driveline wound monitoring, dressing and immobilization are performed frequently by a trained person.	I	C	[71, 259, 363–376]
Driveline dressing should be changed by patients with mechanical circulatory support and/or their family members and/or their caregivers only if all of them are well-trained.	I	C	[71, 259, 363–376]
Heart failure medication after implantation of a left ventricular assist device			
Heart failure medication (diuretic agents, angiotensin converting enzyme inhibitor or angiotensin receptor blocker, beta-blockers and mineralocorticoid receptor antagonists) should be considered during mechanical circulatory support.	IIa	C	[71, 377–384, 393–400]
Driving with a ventricular assist device			
Evaluation and approval of driving ability by a mechanical circulatory support physician are recommended.	I	C	[386–391]
Remote monitoring			
Remote monitoring technology as a supplement to, rather than a substitute for, routine clinical visits for follow-up of patients with long-term mechanical circulatory support may be considered.	IIb	C	[71, 359–362]

16. MYOCARDIAL RECOVERY

Myocardial recovery reportedly occurs in 5–10% of patients supported with CF assist devices, with higher recovery rates after longer support periods [9, 401]. Myocardial recovery is most likely to occur in patients with dilative cardiomyopathy, myocarditis and peripartum cardiomyopathy [393]. Younger patient age and shorter duration of disease are predictors for myocardial recovery [393]. Myocardial recovery, however, is unlikely in patients with ischaemic cardiomyopathy. Different pharmacological therapies to promote myocardial recovery have been proposed. Clearly, continuation and optimization of medical HF therapy and neurohumoral blockage are indicated in potential recovery candidates [71, 398, 402]. Certain subtypes of myocarditis and peripartum cardiomyopathy also respond to medical treatment [403, 404]. Various protocols to identify recovery candidates suitable for weaning from LT-MCS have been proposed [393, 405].

16.1 Evidence review

All patients with non-ischaemic cardiomyopathy should be treated as potential bridge-to-recovery candidates. Despite having the potential effect of myocardial hypertrophy, the addition of the beta-2 adrenergic agonist clenbuterol to standard HF therapy has not been shown to be effective in promoting recovery. At the time of LT-MCS implantation, potential myocardial recovery and device weaning should be anticipated [71]. Significant heart valve diseases that will not improve after LT-MCS implantation should be addressed, and the prevention of adhesions that facilitate device explantation should be considered [71]. Myocardial tissue that is typically retrieved during apical coring should undergo histological processing to identify treatable forms of myocarditis and assess the possibility of myocardial recovery.

To identify myocardial recovery, a standardized screening protocol should be used [393]. Accordingly, patients should undergo routine echocardiographic screening during outpatient visits at regular intervals. Specifically, ventricular function, shape and dimensions should be assessed in a quantitative manner [393]. In the setting of sinus rhythm and complete ventricular remodelling (left ventricular end-diastolic diameter ≤55 mm; left ventricular ejection fraction ≥45%), patients should be evaluated with echocardiography at reduced pump speed for weaning eligibility. If the findings are favourable and sustained, the patients may progress to invasive testing [393], which may include right heart catheterization with the pump speed reduced to the lowest possible level for 15 min. Some centres have stopped using the LVAD and balloon-occluded the outflow graft [406, 407]. Thresholds for device explantation are cardiac index >2.6 l/min/m^2, pulmonary artery wedge pressure (mean)

<16 mmHg, right atrial pressure (mean) <10 mmHg [393, 406]. Adequate anticoagulation must be ensured.

Different strategies for LT-MCS explant have been described. Depending on the individual patient's situation and surgical preference, isolated removal of the pump and driveline or complete device explantation might be appropriate [408]. In patients in critical condition or patients with a high surgical risk (e.g. frailty), ligation of the outflow graft through the subxyphoidal approach or coiling in the catheterization laboratory with cutting of the driveline below the skin without pump explantation might be advisable (decommissioning) [409]. However, this technique necessitates lifelong anticoagulation because the inflow cannula remains in the ventricle. Complete system explantation should be the standard approach for patients with device infection [408].

After LT-MCS explant for myocardial recovery, patients should receive lifelong treatment by HF specialists to target medical therapy and identify recurrence of HF.

Recommendations for the evaluation of myocardial recovery

Recommendations	Class	Level	References
Pathological evaluation of myocardial tissue obtained during apical coring to identify treatable aetiologies of heart failure is recommended.	I	C	[410, 411]
In patients with LT-MCS with non-ischaemic cardiomyopathy, optimized medical heart failure therapy to promote myocardial recovery is recommended.	I	C	[405]
Adding a selective beta-2 adrenergic agonist to conventional HF therapy is not recommended.	III	B	
Routine screening of patients with LT-MCS with non-ischaemic cardiomyopathy for myocardial recovery by echocardiography, including the ramp test, is recommended.	I	B	[397, 412]
Before explantation, invasive haemodynamic examination of patients with LT-MCS is recommended.	I	B	[398]
Cardiopulmonary exercise testing may be considered prior to the decision about LT-MCS explantation.	IIb	C	[413]
Screening for recurrence of heart failure after LT-MCS explantation is recommended.	I	C	[414, 415]

LT-MCS: long-term mechanical circulatory support.

17. PUMP THROMBOSIS AND OTHER LATE ADVERSE EVENTS

Despite improvements in the technical design of LT-MCS devices and the clinical management of patients on LT-MCS, late complications commonly result in hospital admissions.

Late complications of LT-MCS, either ascribed to the pump itself or to the interactions between the pump and the patient, are classified as follows:

1. Complications intrinsic to the pump
   a. Driveline
   b. Pump malfunction
   c. Outflow graft occlusion
2. Complications related to pump-patient interface
   a. Pump thrombosis
   b. GI bleeding
   c. Cerebral vascular accident (CVA) (intracranial haemorrhage, stroke)
   d. Arrhythmia

17.1 Complications intrinsic to the pump

Background and description of the evidence. A total of 13% of device failures are caused by internal pump failure, whereas over 60% are caused by the failure of batteries, the controller and the peripheral cable [416]. Damage to the driveline that interferes with the operation of the pump is a rare, but life-threatening complication. It is often caused by fracture due to accidental mechanical impact. Continuous stress on the cable due to growing body size with weight gain is a risk factor. Moreover, accidental pulling of the cable by dropping the controller bag or by patient falls risks cable damage [417]. Intentional cutting or disconnection of the driveline from the controller has also been described [418]. Treatment of the majority of lead fractures is a simple repair. If the damaged driveline cannot not be repaired, it could require pump explant or exchange, high-urgency HTx, or it could result in patient death.

Pump malfunction is mainly a consequence of pump thrombosis, but technical failure of the broader system components, including the controller, the batteries and the connectors does occur. Technical failure of pulsatile pneumatically driven assist devices has a higher incidence than that of CF-LVADs. Briefly, stoppage of a TAH pump due to membrane rupture is a fatal event; Berlin Heart EXCOR allows substitution of the failing external component but not restarting of the pump in case of a pump stop.

17.2 Complications related to pump-patient interface

Background and description of the evidence. Thrombosis may involve different parts of the MCS, any of which requires specific treatment. Blood flow may be disturbed at different levels of the LVAD system, such as obstruction of the inflow cannula by ingested thrombus (prepump thrombosis), thrombus trapped between the impeller and the housing (intrapump thrombosis) and kinking or stenosis of the outflow graft (post-pump thrombosis). Outflow graft occlusion may be due to stenosis, thrombosis or torsion and may lead to gradual reductions in flow and eventual flow cessation with consequent HF symptoms or death [419, 420].

Diagnosis encompasses clinical signs, pump parameters, laboratory analyses and imaging. Usually, patients with pump thrombus present with various degrees of circulatory compromise and

pump alarms. Log-file analysis of the pump can distinguish between different kinds of blood flow obstructions. The major discriminant is power consumption: High power consumption is a sign of intrapump thrombosis because of the high level of energy needed to produce the same amount of flow in the presence of material-altering rotor movements. Low power consumption translates into low flow alarms for any CF-LVAD. Software is required to analyse the log-files downloaded from the pump, including data concerning the pattern of the pump's power consumption and blood flow throughout the time of symptom onset.

The most common clinical sign of intrapump thrombosis is haemolysis. Haemodynamic instability and new-onset HF are signs of pre- and post-pump thrombosis. Neurological events, any pump flow abnormalities or any other thromboembolic complications should be investigated.

Diagnostic tests for blood flow obstruction across the system are ramp-test echocardiography [421, 422], computed tomographic scans and angiography. Echocardiography can be easily combined with clinical and invasive parameters to evaluate the performance of the LT-MCS device. Echocardiography is appropriate for testing the function of the pump, especially during changes in pump speed in conjunction with haemodynamic monitoring. An enlarged LV and opening of the aortic valve, in combination with wide arterial pulse pressure, is suggestive of blood-flow obstruction, even if the console is showing high power consumption and flow. Echocardiography permits a second-level in-depth analysis: measurement of the peak continuous wave Doppler velocity of the LVAD outflow tract (normal value for HeartMate II <2.7 m/s, <3.4 m/s for HeartWare ventricular assist device (HVAD)) and the ramp test. Standard echocardiographic measurements for ramp studies have been published for HeartMate II and HVAD: Blunted reduction of the left ventricular end-diastolic diameter in response to an increase in pump speed indicates an obstruction of flow through the device [421, 423]. A computed tomography scan with contrast is a valuable tool for the visualization of the LV, inflow cannula and outflow graft.

The definitive treatment of prepump thrombosis is surgical pump exchange, although medical therapy (thrombolysis, glycoprotein inhibitors, unfractionated heparin) may be applied in select cases [424]. Intrapump thrombosis should be treated with lysis, with pump exchange or an urgent transplant if possible [424–426]. Post-pump thrombosis can be treated with stenting of the outflow graft [427]. Cases of kinking or twisting of the outflow graft should be surgically corrected with untwisting of the graft or pump exchange, because stenting is not useful [420]. The recommendations are presented regarding HeartMate II (Abbott, Lake Bluff, IL, USA), HeartWare HVAD (Medtronic, Minneapolis, MN, USA) and HeartMate 3 (Abbott); no data are reported for the Jarvik Flowmaker (Jarvik Heart Inc., New York, NY, USA), HeartAssist 5 (ReliantHeart Inc., Houston, TX, USA) and Berlin Heart INCOR (Berlin Heart GmbH, Berlin, Germany), or other devices. The reported incidence of pump thrombosis is substantially lower for HeartMate 3 compared to HeartMate II [2a] and supposedly the HeartWare HVAD, although a prospective head-to-head comparison of the HeartMate 3 and the HeartWare HVAD has not yet been performed.

17.3 Gastrointestinal bleeding

Background. GI bleeding is the most common cause of hospital readmission [428] and is observed early and late after implantation. Reported incidences range between 5% and 34%.

Description of the evidence. The incidence of GI bleeding is comparable between patients supported with different CF-LVADs. Upper and lower GI endoscopies are the mainstay of initial investigations. Angiography and radionuclide imaging are best suited for acute overt GI bleeding. Capsule endoscopy may play a role in the diagnosis of obscure GI bleeding, usually from the small bowel. Diagnosis and concomitant treatment are possible once the bleeding source is identified. Despite this, no active bleeding site is identified in 30–50% of the cases [344, 429], and it is often then assumed that the site of the bleeding is the small intestine, where arterio-venous malformations are difficult to identify and treat. The primary treatment goal is to stabilize the patient; blood transfusions may be required. Anticoagulation therapy is often interrupted until bleeding is resolved. Recurrent GI bleeding warrants complete withdrawal of antiplatelet therapy and setting a lower target INR, acknowledging the possible increased risk of thromboembolic complications. There are positive reports of the use of octreotide and thalidomide in treating occult and recurrent GI bleeding [430, 431]. However, these drugs are not commonly used in some European countries and there is limited long-term experience. Discontinuation of antithrombotic and antiplatelet therapy poses a potential prothrombotic risk that has to be balanced against the risk of recurrent bleeding episodes [432].

17.4 Cerebral vascular accidents, intracranial haemorrhages and strokes

Background. Thromboembolic complications are the clinical consequences of inadequate haemocompatibility of currently implanted LVADs, a phenomenon of unbalanced interactions between the patient and the pump at different levels that leads to haemorrhagic or ischaemic complications. Ischaemic stroke is more common than intracerebral haemorrhage, but the latter is more likely to be disabling or fatal.

Description of the evidence. CVAs are described for all types of devices, and the reported incidences with modern devices remain high [145]. Overall incidence ranges from 6.7% to 29.7% (0.07 to more than 0.26 events per patient year). BP management is of primary importance: mean arterial pressure higher than 90 mmHg is associated with a risk of stroke during CF-LVAD support [146, 433]. Doppler BP measurement is the gold standard, and it reflects systolic BP. Antiplatelet and antithrombotic therapies are crucial as prophylaxis against CVA: Use of aspirin and strict anticoagulation monitoring are protective for CVA.

The clinical management, diagnostic procedures and treatment of CVA in patients with LT-MCS follow standard clinical practice. Systemic thrombolysis is not recommended for patients on LVAD due to the unacceptably high risk of bleeding.

Instead endovascular interventions for acute ischaemic stroke are warranted. Evidence from large trials suggests that lowering BP decreased the incidence of stroke [146, 433]. Strict outpatient management of BP is effective, considering that the risk of stroke is shown to increase from 9 to 12 months post implant [377, 434].

17.5 Arrhythmia

Background. Arrhythmias are frequent during LT-MCS and a common cause of hospitalization. Ventricular and atrial arrhythmias are often a manifestation of the underlying disease and frequently present preoperatively. Several precipitating factors contribute to early postoperative arrhythmia [435].

Description of the evidence. The burden of VA in LT-MCS recipients is high; preoperative VA is the major predictor of late postoperative VA. VA is reasonably tolerated by many patients supported by LT-MCS with a low risk of immediate haemodynamic collapse [436]. The role of implantable cardioverter defibrillators (ICDs) for primary prevention of sudden cardiac death is unclear in patients supported by LT-MCS [84, 437]. Definitive data are not available: The largest retrospective study included mostly pulsatile devices, and the conclusions are not directly translatable to CF-LVAD [438]. For a subgroup of patients who present with a history of refractory VAs, aggressive antiarrhythmic therapy and catheter ablation are indicated.

Atrial fibrillation is also common in patients with LT-MCS. The effect on outcome and risk of thromboembolism is relevant. Pharmacological rhythm control strategy is widely accepted; other procedures (catheter ablation, left appendage closure) have limited evidence. Pharmacological treatment is indicated, and catheter ablation may be attempted in cases of sustained or recurrent VA. In patients with an ICD implanted prior to LT-MCS implantation, ventricular tachycardia therapy should be active to prevent adverse sequelae of right ventricular dysfunction. However, ICD settings should be very conservative. Less evidence exists for primary prevention ICD in patients without arrhythmia at the time of LVAD implantation. It might be considered not to replace a depleted ICD battery in the absence of VAs. ICD implantation is indicated for patients with LT-MCS who develop postoperative VA with haemodynamic deterioration.

Recommendations for pump thrombosis and other late adverse events

Recommendation	Class	Level	References
Device malfunction			
It is recommended that out-patient management encompass regular evaluation and inspection of the technical parameters and all components of the external part of the device and their connections.	I	C	[416]
It is recommended that in cases of pump malfunction with clinical symptoms, the patient is assisted by emergency medical service and referred to the implanting centre.	I	C	[417, 418]
Surveillance by abdominal radiogram to regularly assess internal components of the driveline may be considered.	IIb	C	
In case of damage to the external parts of the driveline, splice repair of the wires in the operating room by technical personnel, with a surgery team on standby, should be considered.	IIa	C	[439]
In-hospital evaluation is recommended for pump alarms signalling pump malfunction.	I	C	
Pump thrombosis			
In the case of a clinical thrombotic event, pump evaluation for device thrombosis is recommended.	I	C	[422, 440]
Evaluation of the presence of pump thrombosis is recommended if flow alarms are present.	I	C	[422, 440]
In the case of a flow obstruction, technical, clinical and diagnostic investigations of the outflow graft, pump body and inflow cannula are recommended.	I	C	[422, 440]
Routine monitoring of lactate dehydrogenase and plasma free haemoglobin levels during follow-up is recommended.	I	C	[441]
In the case of pump thrombosis of a HeartWare HVAD, device exchange should be considered.	IIa	C	[424, 426]
In the case of pump thrombosis of a HeartWare HVAD, thrombolysis may be considered.	IIb	C	[424, 426]
In the case of pump thrombosis of a HeartMate II, device exchange or a high-urgency heart transplant (if possible) should be considered.	IIa	C	[424]
In a scenario of prepump (inflow graft) thrombosis, a backwash with carotid artery protection may be considered.	IIb	C	[442]
In a scenario of post-pump (outflow graft) thrombosis, stenting should be considered.	IIa	C	[422, 427, 443–446]

Continued

Recommendations for pump thrombosis and other late adverse events *(Continued)*

Events of bleeding during LT-MCS			
For a major bleeding event, temporary discontinuation of anticoagulation therapy is recommended.	I	C	
For a critical clinical bleeding episode or if the international normalized ratio is >4, anticoagulation reversal is recommended.	I	C	
If gastrointestinal bleeding is recurrent, discontinuation of platelet inhibitors should be considered.	IIa	C	[428]
Evaluation of other causative factors that might influence the risk of gastrointestinal bleeding should be considered.	IIa	C	[35, 117, 447–449]
In cases of occult recurrent bleeding despite the use of the above measures, octreotide or thalidomide may be considered.	IIb	C	[430, 431]
Prevention and treatment of cerebrovascular accidents			
A target mean arterial pressure <85 mmHg to reduce the risk of stroke is recommended.	I	B	[377, 433, 434]
Computed tomography angiography is recommended for vascular imaging and endovascular treatment of ischaemic stroke.	I	A	[450]
In cases of acute neurological deficit, emergent neuroimaging with computed tomographic scans is recommended.	I	A	[450]
Reversal of coagulopathy with prothrombin complex concentrates or transfusions with fresh frozen plasma and platelets is recommended for treatment of haemorrhagic stroke.	I	A	[451, 452]
Cardiac arrhythmias			
In patients with long-term mechanical circulatory support who develop postoperative ventricular arrhythmia with haemodynamic compromise, ICD implantation is recommended.	I	C	[438]
To prevent adverse sequelae of right ventricular dysfunction, continuation of ICD therapy should be considered.	IIa	C	[435]
Prophylactic ICD implantation in patients without arrhythmias at the time of long-term mechanical circulatory support implantation is not recommended.	III	C	[437, 438, 453]

ICD: implantable cardioverter defibrillator; LT-MCS: long-term mechanical circulatory support.

18. AORTIC INSUFFICIENCY AND LATE RIGHT HEART FAILURE

18.1 Background

Under LVAD support, de novo aortic insufficiency can develop. The incidence varies in different publications from 10% [454] to 53% [384]. Recirculating blood will lead to systemic hypoperfusion of the patient. Additionally, incomplete unloading of the LV may lead to pulmonary artery hypertension compromising the RV function. Factors contributing to AR are fusion of the commissures and degenerative changes of the cusps caused by persistent aortic valve closure [455]. The diagnosis and the grade of regurgitation can be confirmed by echocardiography.

18.2 Evidence review

Factors that influenced AR development and progression were older age, persistent aortic valve closure, duration of LVAD support and female gender [456]. Treatment options include HTx, bioprosthetic valve replacement, patch closure or valve repairs. Transcatheter procedures have been shown to be effective for patients in whom the risk of reoperation is prohibitive [456–461].

Recommendations for aortic insufficiency

Recommendations	Class	Level	References
Diagnosis			
Echocardiography for routine follow-up of aortic valve function is recommended.	I	C	[460, 462]
The ramp test to diagnose aortic insufficiency should be considered.	IIa	C	[463]
Treatment of moderate aortic insufficiency			
Variation in pump speed settings to reduce aortic insufficiency should be considered.	IIa	B	[68]
A heart transplant is recommended.	I	C	
Open valve replacement or closure of an insufficient aortic valve is not recommended.	III	C	

Continued

Recommendations for aortic insufficiency *(Continued)*

Interventional closure of the aortic valve may be considered.	IIb	C	[458, 461, 464]
Transcatheter aortic valve replacement should be considered.	IIa	C	[461, 465, 466]
Treatment of severe aortic insufficiency			
Reduction in pump speed settings to reduce aortic insufficiency may be considered.	IIb	C	[68]
High-urgent listing for a heart transplant is recommended if the patient is a transplant candidate.	I	C	
Open valve replacement or closure of the insufficient aortic valve may be considered.	IIb	C	[457, 467]
Interventional closure of the aortic valve may be considered.	IIb	C	[458, 461, 464]
Transcatheter aortic valve replacement should be considered.	IIa	C	[461, 465, 466]

18.3 Late right heart failure

Currently there is no established definition of late onset right ventricular failure (LORVF). Although in 2 studies LORVF was defined as the need for inotropic support or RVAD implantation starting 14 days after surgery, another study defined LORVF as a readmission requiring medical or surgical intervention [177, 468, 469].

18.4 Evidence review

In a large analysis of the INTERMACS database including 10 909 adult patients with primary LVAD support, the incidence of LORVF (>14 days) was 6.4% [468].

In a retrospective single-centre study including 336 patients, the incidence of LORVF was 11%. In these patients, diabetes mellitus, a body mass index >29 and blood urea nitrogen level >41 mg/dl were significant predictors of LORVF [469].

Recommendations for late right heart failure

Recommendations	Class	Level	References
Diagnosis			
Routine follow-up echocardiography for assessment of right heart function is recommended.	I	C	
Invasive haemodynamic measurements should be considered.	IIa	C	[470]
Treatment			
Initial treatment for right heart failure with diuretics is recommended.	I	C	
Medical lowering of pulmonary resistance may be considered.	IIb	C	[471]
High-urgent listing for a heart transplant is recommended if the patient is a transplant candidate.	I	C	
Secondary right ventricular assist device implantation may be considered.	IIb	C	

Diagnostic investigations of LORVF should include echocardiography and invasive haemodynamic measurements with a pulmonary artery catheter.

19. INFECTION

Infection remains a major source of morbidity and mortality in patients with MCS despite significant progress in the development of more durable VADs and advances in surgical techniques over the last decade [25, 176]. The most recent INTERMACS report showed that infection was still the fourth most common cause of death within 1 year after implant [25]. The International Society of Heart and Lung Transplantation recognized the importance of clearly defining infection in this unique population and commissioned an international working group of experts to develop definitions of infection in patients with MCS that were published in 2011 [363]. Hence, these international definitions are recommended for defining infection in Europe and are part of this European consensus document.

19.1 Evidence for preventing infection in preimplantation of mechanical circulatory support

Nosocomial bloodstream infection (BSI) has been reported as a major source of morbidity and mortality in patients with MCS [472]. In general the risk of infection associated with catheters depends on type, location and duration *in situ* [473]. A recent study from the International Society of Heart and Lung Transplantation IMACS Registry, to which the EUROMACS Registry contributes, showed that early-onset BSI was associated with a significantly increased 24-month mortality rate and that 85% of these BSIs were not device related. There is an opportunity for infection prevention practices to decrease the BSI event rate in the intensive care unit and post-surgical settings, which may affect the 24-month survival rate [474].

Catheter-associated urinary tract infection is the most common nosocomial infection and is preventable by limiting the number of days of catheterization. As with indwelling catheters, a general proactive approach in patients with MCS of changing or reducing the duration of the catheters where possible to reduce the risk of infection is recommended as per other intensive care unit and post-surgical patients [475].

19.2 Evidence for antimicrobial prophylaxis perioperatively

In earlier studies, antimicrobial prophylaxis was broad spectrum and given for a prolonged duration. Two published multicentre surveys reported a wide variation in the different types of antimicrobial prophylaxis used in MCS implant surgery [476, 477]. More recently, MCS centres follow more general cardiac surgery prophylaxis guidelines and do not include broad spectrum gram-negative or fungal coverage. Cardiac surgery prophylaxis guidelines usually recommend a cephalosporin (cefazolin or cefuroxime) for 24–48 h, which can provide sufficient gram-positive and gram-negative coverage [26, 478–481]. Routine antifungal prophylaxis is not recommended [26].

19.3 Evidence for managing infection in patients with mechanical circulatory support

Whenever clinically feasible, infection should be excluded or appropriately treated before MCS implantation. In candidates for MCS before implantation, evaluation of suspected infection is no different from that in other patients and should be guided by clinical signs and symptoms. In patients with unexplained fever and/or leucocytosis, evaluation should include blood cultures, urinalysis, urine culture and chest radiogram, with additional imaging as needed until a diagnosis is established and the source has been treated and cleared. In all MCS candidates with suspected or proven infection, expert infection consultation is advisable. MCS candidates with BSI should be treated with targeted antimicrobial therapy [363].

For an active infection, there is insufficient evidence to define a minimum duration of antimicrobial therapy before proceeding to MCS implantation [26]. However, delaying MCS implantation is recommended where feasible until the following general goals are met: control of the source (e.g. incision and drainage of abscess, removal of infected catheter or tooth extraction for dental abscess); blood culture results have become negative after appropriate antibiotic treatment commenced; and illness and sepsis are resolved. Candidates for MCS with other infections (e.g. pneumonia, urinary tract infection) should be treated with appropriate antimicrobial therapy until resolution. Expert infection consultation should be sought in all cases of infection preimplantation and throughout the perioperative period.

19.4 Evidence for assessing a patient for postoperative infection after implantation of mechanical circulatory support

The initial evaluation should include a careful history and review of symptoms. Physical examination of surgical wounds, driveline exit site and review of the LT-MCS device function are essential because early detection and treatment of a localized process may prevent progression to more serious VAD infections [26, 363].

In case of driveline exit site infection, the treatment includes increased frequency of dressing change, topical antiseptics and prolonged or lifelong antibiotics (suppressive treatment). In case of ascending driveline infection, surgical revision may be an option.

Recommendations for prevention and treatment of infections preimplant and postimplant

Recommendations	Class	Level	References
Infection prevention prior to LT-MCS implant			
If time and clinical status permit, removal or exchange of all central venous catheters, pulmonary vein catheters and urine catheter prior to LT-MCS device implantation is recommended.	I	C	[474, 482–484]
If time and clinical status permit, a dental assessment and therapy if required prior to LT-MCS device implantation, are recommended.	I	C	[485]
A nasal and groin screen for methicillin-resistant *Staphylococcus aureus* and, if positive, treatment with topical antibiotics prior to LT-MCS device implantation, are recommended.	I	C	[486, 487]
Antibiotic prophylaxis			
Preoperative antimicrobial prophylaxis targeted at *Staphylococcus* sp. and methicillin-resistant *S. aureus* (in patients with positive test results) is recommended.	I	C	[478–480]
The inclusion of antifungal treatment in routine preoperative antimicrobial prophylaxis is not recommended.	III	C	[488, 489]
It is recommended that antibiotic prophylaxis be administered within 60 min of the first incision, remain in the therapeutic range throughout its use and not be extended beyond 24 h after surgery.	I	C	[479, 490]
Managing active infection preimplant			
In patients with active infections prior to LT-MCS device implantation, antibiotic therapy as directed by an infectious disease expert is recommended.	I	C	[363]

Continued

Recommendations for prevention and treatment of infections preimplant and postimplant *(Continued)*

Infective endocarditis treatment preimplant			
Documented clearance (negative blood culture results) of patients who have had bacteraemia prior to LT-MCS device implantation is recommended.	I	C	
In patients with bacteraemia, antimicrobial therapy for at least 7 days prior to implantation of a mechanical circulatory support device is recommended.	I	C	
In patients with bloodstream infections not related to infective endocarditis, removal of sources (if known) and antimicrobial treatment are recommended.	I	C	
LT-MCS implantation in patients with untreated acute infective endocarditis with active bacteraemia is not recommended.	III	C	
Preventing infection postimplant			
It is recommended that the velour part of the driveline not exit the body.	I	C	[259]
Stabilization of the driveline immediately after the device is implanted and continuing throughout the duration of support is recommended.	I	C	[491]
A dressing change protocol initiated immediately postoperatively is recommended.	I	B	[491, 492]
Secondary antibiotic prophylaxis for the prevention of infectious events during routine procedures and dental work due to the risk of bacteraemia should be considered.	IIa	C	[71, 493, 494]
Evaluation of patients with mechanical circulatory support with a suspected infection			
In all patients, a complete blood count, chest radiographic images and blood cultures are recommended.	I	C	[363]
It is recommended to draw at least 3 sets of blood cultures over 24 h, with at least 1 culture from any indwelling central venous catheter.	I	C	[363]
For those with a suspected pump cannula or driveline infection, obtaining a sample for gram stain, the KOH test and routine bacterial and fungal cultures are recommended.	I	C	[363]
When clinically indicated, an aspirate from other potential sources, as dictated by presenting symptoms and examination, is recommended.	I	C	[363]
Directed radiographic studies based on presenting symptoms and examination are recommended.	I	C	[363]
Erythrocyte sedimentation rate or serial C-reactive protein should be considered.	IIa	C	[363]
Routine computed tomography of the chest, abdomen and pelvis is not recommended.	III	C	[363]
Leucocyte radiolabelled scintigraphy may be considered to identify deep infections but by itself lacks anatomical specificity.	IIb	C	[495]
Combining single positron emission tomography/computed tomography scans with radiolabelled leucocytes has increased the sensitivity for detection of infection and retained the specificity for anatomical location of the MCS infection; it can also identify distal foci if infected emboli are present and should be considered.	IIa	C	[496, 497]
Treatment of patients with mechanical circulatory support with a suspected infection of the driveline exit site or the driveline itself			
A full evaluation as outlined above should be performed in all patients prior to treatment before commencing antimicrobial treatment even if only superficial infection is suspected.	I	C	[363]
In patients with a superficial driveline exit site infection but without a BSI or systemic illness, it is recommended that antibiotic therapy be deferred until culture results are known.	I	C	[71, 498, 499]
In patients with clinical signs of driveline exit site infection but with negative culture results, initiation of empirical oral antibiotic therapy and evaluation based on clinical response are recommended.	I	C	
In the presence of systemic illness and/or sepsis, initiation of empirical intravenous antibacterial therapy always covering *Staphylococcus, Pseudomonas* and *Enterobacteriaceae* species, also taking local institutional epidemiology and colonization (e.g. methicillin-resistant *Staphylococcus aureus*, vancomycin-resistant *Enterococci*) into consideration, is recommended.	I	C	
Rifampicin should usually be avoided due to its significant impact on the international normalized ratio, but it may be considered in rare cases.	IIb	C	[500]
It is recommended that the duration of antimicrobial treatment be guided by the clinical response, type of infection, pathogen(s), transplant status and the opinion of an infectious disease expert.	I	C	
It is recommended that the treatment of a superficial infection without an associated BSI last at least 2 weeks.	I	C	
For deep infections, treatment for at least 6 weeks, depending on the pathogen, time to clearance of the BSI, the clinical response and the expert opinion of an infection disease expert, are recommended.	I	C	[26]

Continued

Recommendations for prevention and treatment of infections preimplant and postimplant *(Continued)*

Single positron emission tomography/computed tomography combined with radiolabelled leucocytes for the detection of location of infection and infected emboli should be considered.	IIa	C	[496, 497]
Leucocyte radiolabelled scintigraphy for identification of deep infection may be considered.	IIb	C	[495]
If the infection is not eradicated despite debridement and 6 weeks of systemic intravenous antibiotic treatment, specific surgical treatment of the infections should be considered, including driveline relocation, pump exchange, prolonged treatment of the ventricular assist device, wrapping driveline with omentum and a heart transplant.	IIa	C	
Lifelong antibiotic treatment for complicated *S. aureus* infection should be considered unless there is an option to remove the device.	IIa	C	
Treatment of patients with mechanical circulatory support with a suspected infection of the pump			
In all patients with mechanical circulatory support, a full evaluation for any suspected infection as outlined above should be performed before commencing antimicrobial treatment.	I	C	[26, 363]
In the case of a persistent bloodstream infection, pump seeding or endovascular infection should be suspected. It is recommended that intravenous antimicrobial therapy be initiated after microbiological samples have been taken.	I	C	
For infection in patients with mechanical circulatory support at the time of device exchange or heart transplant, it is recommended that antimicrobial therapy be continued for at least 6 weeks, depending on the pathogen and the clinical course, to minimize the risk of relapse.	I	C	[26]
After failure of eradication of infection with debridement and 6 weeks of systemic intravenous antibiotic treatment, specific surgical treatment of infections including pump exchange and a heart transplant should be considered.	IIa	C	

LT-MCS: long-term mechanical circulatory support; BSI: bloodstream infection.

20. END-OF-LIFE CARE

20.1 Introduction

Optimal care of patients with LT-MCS, especially those in whom it is a destination therapy, has to include comprehensive end-of-life (EOL) considerations. When life-prolonging therapy can be expected to cause more suffering than benefit, palliative care (PC) should focus on quality of life and an easy death in accordance with the patient's wishes.

Taking care of patients with LT-MCS as a destination therapy can be more difficult than taking care of HTx candidates or HTx patients [501–504]. Factors that can complicate advanced HF management such as ageing-related comorbidities, end-organ damage, cognitive impairment, frailty and limited social support are compounded by risk of MCS failure and MCS-related complications such as bleeding, infection and stroke. As a result, LT-MCS is associated with repeated hospitalizations and a high rate of caregiver burnout. The unpredictable course of advanced HF, differences among LT-MCS devices and a limited evidence base can further complicate shared decision-making, preparedness planning and EOL care [503].

Successful PC requires a multidisciplinary approach with fluid communication between the patient and caregivers on the one hand, and between primary care services, the LT-MCS team and PC specialists on the other [9, 71, 505, 506].

20.2 Review

For best EOL care, PC should begin before implantation of the MCS device and continue throughout the duration of support, especially for patients with increasing comorbidities [502]. The main goals of PC for patients with LT-MCS are management of symptoms, psychosocial issues and spiritual concerns. Therefore, although communication with patients with advanced HF is complex due to the highly unpredictable course of the disease, among other things, there should ideally be a discussion with the patient and caregivers about expectations, goals and EOL preferences during the evaluation of patients for destination therapy LT-MCS. This discussion should lead to a comprehensive EOL plan, focusing on conditions for withdrawal of MCS or related medications, such as anticoagulation, being drawn up preoperatively and made available to all relevant parties [502, 504]. An advance health care directive, also known as a living will, including designation of a proxy decision maker for when the patient is unable to make his or her own decisions, can be a great help [507]. However, the plan should be re-evaluated whenever necessary, since the patient's acceptance of aggressive treatments may change. Life-prolonging support may be discontinued with the patient in the hospital, in a hospice for terminal patients or at home. However, it should be pointed out that hospice care prior to withdrawal may be problematic, since many hospice staff lack experience and training with MCS therapies [502].

20.3 Symptom management

These patients often experience pain, which can be of multifactorial origin but frequently affects skeletal muscle and which can be aggravated by the presence of the LT-MCS device. For pain management, opioids have advantages over non-steroidal anti-inflammatory drugs, since the latter affect renal function and volume status and increase the risk of GI bleeding. Mood disorders such as anxiety and depression are very common as well, the treatment of which, whether pharmacological or otherwise, may require referral to a mental health specialist. In such cases there can be a risk of suicide, because the patient has direct access to the life-supporting device [502]. Other frequent symptoms that must be addressed include anorexia, constipation and insomnia.

20.4 Psychosocial and spiritual concerns

The single-centre Palliative Care in Heart Failure (PAL-HF) trial showed that interdisciplinary PC of patients with advanced HF afforded better quality of life and spiritual well-being, less anxiety and lower risk of depression than conventional care [508].

20.5 Device-specific and physiological considerations

The health professionals and/or caregivers who provide EOL care must have specific training in defibrillator deactivation, the minimization of VAD alarms and VAD deactivation and an understanding of residual native heart function, which allows estimation of how long the patient will survive following deactivation.

Recommendations for end-of-life care

Recommendations	Class	Level	References
A discussion of palliative care, potential complications, expectations and advance health care directives prior to implantation of a long-term mechanical circulatory support device is recommended.	I	C	[71, 502, 507]
Managing quality-of-life issues in a multidisciplinary palliative care team throughout the remainder of the patient's life is recommended.	I	C	
The development of institution-specific protocols for the collaboration of the mechanical circulatory support team, palliative care specialist and social workers in the eventual deactivation of the mechanical circulatory support device in the final tranche of the end-of-life period should be considered.	IIa	B	[502, 507]

SUPPLEMENTARY MATERIAL

Supplementary material is available at *EJCTS* online.

ACKNOWLEDGEMENTS

The authors would like to thank Rianne Kalkman for her expertise and help in writing and reviewing this expert consensus.

Conflict of interest: Evgenij V. Potapov: Institutional research and travel grants, consulting and proctoring fees from Abbott and Medtronic. Maria G. Crespo-Leiro: Research support from Novartis, Vifor Pharma, and FEDER Funds; personal fees (travel grants, lecture fees and/or advisory boards) from Novartis, Abbott Vascular, Astellas, MSD, Amgen, Sanofi and Servier. Lars H. Lund: Speaker's honoraria from Abbott. Ivan Netuka: Consultant, grant, advisory board Abbott; USA; advisory board and a principal investigator of the CE Mark Study Carmat SA, France; advisory board EvaHeart Inc., USA; advisory board, stockholder LeviticusCardio Ltd, Israel. Steven Tsui: Consultant for CorWave Ltd and 3R Ltd; research support from Maquet Getinge group. Daniel Zimpfer: Proctor, advisor, research and travel grants from Abbott and Medtronic. Finn Gustafsson: Advisor: Carmat, Corvia, Pfizer. Speaker: Abbott, Orion Pharma, Novartis. The other authors have no conflict of interest to disclose.

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