

## 2019 EACTS Expert Consensus on long-term mechanical circulatory support

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

<sup>a</sup> Department of Cardiothoracic and Vascular Surgery, German Heart Center Berlin, Germany; DZHK (German Centre for Cardiovascular Research), Partner Site Berlin, Germany

<sup>b</sup> Department of Cardiothoracic Surgery, Erasmus University Medical Center, Rotterdam, Netherlands

<sup>c</sup> Complejo Hospitalario Universitario A Coruña (CHUAC), Instituto de Investigación Biomédica de A Coruña (INIBIC), CIBERCV, UDC, La Coruña, Spain

<sup>d</sup> Sorbonne Université, INSERM, Institute of Cardiometabolism and Nutrition, Paris, France

<sup>e</sup> Service de médecine intensive-réanimation, Institut de Cardiologie, APHP, Hôpital Pitié-Salpêtrière, Paris, France

<sup>f</sup> Department of Cardiothoracic Surgery, Jena University Hospital, Friedrich-Schiller-University of Jena, Jena, Germany

<sup>g</sup> Department of Medical Microbiology, University College of Dublin, Dublin, Ireland

<sup>h</sup> Department of Anaesthesiology, German Heart Center Berlin, Berlin, Germany

<sup>i</sup> Department of Cardiology, University Medical Center Utrecht, Utrecht, Netherlands

<sup>j</sup> Department of Cardiothoracic, S. Orsola Hospital, Transplantation and Vascular Surgery, University of Bologna, Bologna, Italy

<sup>k</sup> Department of Medicine Karolinska Institute, Heart and Vascular Theme, Karolinska University Hospital, Solna, Sweden

<sup>l</sup> Department of Cardiovascular Surgery Swiss Cardiovascular Center, Inselspital, Bern University Hospital, Bern, Switzerland

<sup>m</sup> Clinic for Thoracic and Cardiovascular Surgery, Herz- und Diabeteszentrum Nordrhein-Westfalen, Bad Oeynhausen, Germany

<sup>n</sup> Institute for Clinical and Experimental Medicine (IKEM), Prague, Czech Republic

<sup>o</sup> Department of Cardiovascular Surgery, Ege University, Izmir, Turkey

<sup>p</sup> Advanced Heart Failure and Mechanical Circulatory Support Program, Cardiac Intensive Care, San Raffaele Hospital, Vita Salute University, Milan, Italy

<sup>q</sup> Department of Anesthesia and Intensive Care, San Raffaele Hospital, Vita Salute University, Milan, Italy

<sup>r</sup> Department of Congenital Pediatric Surgery, Zurich Children's Hospital, Zurich, Switzerland

<sup>s</sup> Royal Papworth Hospital, Cambridge, United Kingdom

<sup>t</sup> Department of Surgery, Division of Cardiac Surgery, Medical University of Vienna, Vienna, Austria

<sup>u</sup> 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

<sup>†</sup>The first two authors contributed equally to this study.

## TABLE OF CONTENTS

1. ABBREVIATIONS AND ACRONYMS .....	2
2. INTRODUCTION .....	2
3. METHODS .....	3
4. PATIENT EVALUATION AND TIMING OF IMPLANTATION .	3
5. PREOPERATIVE ORGAN FUNCTION OPTIMIZATION .....	5
6. CONCOMITANT CARDIAC CONDITIONS INCLUDING	
ARRHYTHMIAS .....	6
7. MANAGEMENT OF NON-CARDIAC COMORBIDITIES .....	7
8. SYSTEM SELECTION .....	9
9. ANAESTHETIC MANAGEMENT .....	11
10. OPERATIVE TECHNIQUE .....	12
11. PAEDIATRIC OPERATIVE TECHNIQUES .....	14
12. POSTOPERATIVE MANAGEMENT IN THE INTENSIVE	
CARE UNIT .....	15
13. ANTICOAGULATION .....	16
14. REHABILITATION .....	18
15. OUTPATIENT CARE .....	18
16. MYOCARDIAL RECOVERY .....	20
17. PUMP THROMBOSIS AND OTHER LATE	
ADVERSE EVENTS .....	21
18. AORTIC INSUFFICIENCY AND LATE	
RIGHT HEART FAILURE .....	24
19. INFECTION .....	25
20. END-OF-LIFE CARE .....	28
SUPPLEMENTARY MATERIAL .....	29
ACKNOWLEDGEMENTS .....	29
REFERENCES .....	29

## 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	<i>Weight of evidence/opinion is in favour of usefulness/efficacy.</i>	Should be considered
Class IIb	<i>Usefulness/efficacy is less well established by evidence/opinion.</i>	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 ( $\leq 25\%$ ), who were inotropic 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: <ul style="list-style-type: none"> <li>• New York Heart Association functional class IIIB–IV and</li> <li>• Ejection fraction &lt;25% and</li> </ul> At least one of the following criteria: <ul style="list-style-type: none"> <li>○ INTERMACS 2–4</li> <li>○ Inotrope dependence</li> <li>○ Progressive end-organ dysfunction</li> <li>○ Peak VO<sub>2</sub> &lt;12 ml/kg/min</li> <li>○ Temporary MCS dependence</li> </ul>	IIa	B	
LT-MCS implantation may be considered in patients with: <ul style="list-style-type: none"> <li>• New York Heart Association functional class IIIB–IV and</li> <li>• Ejection fraction &lt;25% and <ul style="list-style-type: none"> <li>○ To reverse elevated pulmonary vascular resistance or potentially reversible renal failure in potential heart transplant candidates</li> <li>○ 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</li> </ul> </li> </ul>	IIb	B	
<b>Patient characteristics associated with a high risk of poor outcome post-left ventricular assist device</b>			
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
<b>Renal function</b>			
In patients with renal dysfunction, optimization via improvement of cardiac output and reduction of filling pressures is recommended.	I	B	[56]
<b>Liver function</b>			
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]
<b>Pulmonary function</b>			
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	
<b>Coagulation</b>			
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	
<b>Nutritional, metabolic and endocrine considerations</b>			
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
<b>Aortic valve and root diseases</b>			
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]
<b>Mitral valve disease</b>			
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	
<b>Tricuspid valve disease and right ventricular dysfunction</b>			
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]
<b>Intracardiac shunts</b>			
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 unreparable ventricular septal defect, LT-MCS implantation is not recommended.	III	C	[71]

Continued

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

<b>Arrhythmia</b>			
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	
<b>Intracardiac thrombus</b>			
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	
<b>Miscellaneous conditions</b>			
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 be 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
<b>Malignancies</b>			
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	
<b>Pulmonary hypertension</b>			
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]
<b>Cardiac cachexia</b>			
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*)

<b>Renal dysfunction</b>			
Implantation of long-term mechanical circulatory support should be considered in case of reversible secondary renal dysfunction.	<b>IIa</b>	C	[37, 56, 71, 103]
Implantation of long-term mechanical circulatory support may be considered in patients on chronic haemodialysis.	<b>IIb</b>	C	[37, 56, 103]
<b>Neurological function and disorders</b>			
Careful neurological examination is recommended for all candidates for implantation of long-term mechanical circulatory support including assessment of dementia and mental status.	<b>I</b>	C	[104, 132]
Multidisciplinary evaluation of prognosis of survival and morbidity of patients with neuromuscular disorders is recommended.	<b>I</b>	C	[133]
<b>Adherence (medical therapy, alcohol, tobacco, psychological, psychiatric and social derangement)</b>			
Screening for psychological and psychiatric (including cognitive function) disorders and substance abuse is recommended.	<b>I</b>	C	[104]
It is recommended that adherence (tobacco, alcohol and substance abuse), psychosocial risks and familial support be evaluated.	<b>I</b>	C	[134]
In patients with frailty, psychiatric or neurological disorders, evaluation of their ability to operate the device is recommended.	<b>I</b>	C	
<b>Vascular disease</b>			
Screening for peripheral vascular disease is recommended.	<b>I</b>	C	[67]
<b>Coagulation and haematological disorders</b>			
Evaluation of all long-term mechanical circulatory support candidates for coagulopathies and hypercoagulable states (e.g. thrombophilia) is recommended.	<b>I</b>	C	[135]
In patients with thrombocytopenia after exposure to heparin, testing for heparin-induced thrombocytopenia should be considered.	<b>IIa</b>	C	[136]
<b>Respiratory considerations</b>			
Spirometry as part of the patient work-up should be considered.	<b>IIa</b>	C	[25, 37, 137]
Preoperative thoracic imaging should be considered as part of the overall risk/benefit evaluation.	<b>IIa</b>	C	[25, 37, 137]
<b>Diabetes</b>			
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.	<b>I</b>	C	
Implantation of long-term mechanical circulatory support in patients with diabetes with severe end-organ complications is not recommended.	<b>III</b>	C	
<b>Gastrointestinal disorders</b>			
Gastrointestinal bleeding in patients 50 years or older: faecal occult blood testing, gastroscopy and endoscopy should be considered.	<b>IIa</b>	C	[116, 117]
<b>Pregnancy</b>			
Contraception in women of childbearing age after implant of long-term mechanical circulatory support is recommended.	<b>I</b>	C	
Long-term mechanical circulatory support in the setting of pregnancy is a multidisciplinary challenge and may be considered.	<b>IIb</b>	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 configurations provide comparable outcomes [173]. The insertion of two implantable CF-LVADs as BiVAD configuration is predominately 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 multi-centre 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
<b>Monitoring</b>			
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.	IIIb	C	[225]
Neuromonitoring with near infrared spectroscopy should be considered, especially in off-pump implantation.	IIa	C	[243]
<b>Periprocedural transoesophageal echocardiography</b>			
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]
<b>Assessment of right ventricular failure</b>			
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  $<2.0\text{ l/min/m}^2$ , mixed venous oxygen saturation  $<55\%$  and mean arterial pressure  $<50\text{ mmHg}$  [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  $>400\text{ s}$ . 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
<b>Use of circulatory assistance during implantation: implant strategy</b>			
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]
<b>Mechanical circulatory support site preparation</b>			
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]
<b>Implantable left vascular assist device–inflow cannula placement</b>			
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]
<b>Apical cuff positioning</b>			
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	
<b>Implantable left ventricular assist device: outflow graft</b>			
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]
<b>Implantable left ventricular assist device: alternative implant strategy/left thoracotomy approach</b>			
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]
<b>Driveline externalization</b>			
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]
<b>Air embolism prevention</b>			
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	
<b>Alternative implant surgical strategy</b>			
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	
<b>Closing surgical operation field considerations</b>			
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	
<b>Biventricular support</b>			
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 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]
<b>Long-term paracorporeal support</b>			
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]
<b>Total artificial heart</b>			
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]
<b>Long-term mechanical circulatory support explant</b>			
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<sup>®</sup> 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<sup>2</sup> 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<sup>2</sup> 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
<b>Device selection in small children</b>			
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]
<b>Use of a SynCardia total artificial heart</b>			
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]
<b>Patients with congenital heart disease requiring mechanical circulatory support</b>			
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
<b>Monitoring</b>			
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 <i>in situ</i> 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	
<b>Right ventricular failure in patients with a left ventricular assist device</b>			
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]
<b>Inotrope and vasopressor support</b>			
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]
<b>Postoperative mechanical ventilation</b>			
Avoidance of hypercarbia that increases pulmonary artery pressure and RV afterload is recommended.	I	C	
<b>Bleeding and transfusion management</b>			
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
<b>Management of anticoagulation preoperative, perioperative and postoperative of LT-MCS implantation</b>			
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]
<b>Management of anticoagulation in the event of bleeding episodes</b>			
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  $\text{VO}_2$  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
<b>Mechanical circulatory support programme management</b>			
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]
<b>Successfully discharging a patient with mechanical circulatory support</b>			
Patient and caregiver education/training regarding device management, anticoagulation monitoring and driveline care is recommended.	I	B	[25, 37, 71, 137, 284, 354–360]
<b>Blood pressure management</b>			
In patients with continuous-flow mechanical circulatory support, a mean systemic blood pressure goal of $\leq 85$ mmHg is recommended.	I	B	[71, 377–384]
<b>Driveline dressing management</b>			
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]
<b>Heart failure medication after implantation of a left ventricular assist device</b>			
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]
<b>Driving with a ventricular assist device</b>			
Evaluation and approval of driving ability by a mechanical circulatory support physician are recommended.	I	C	[386–391]
<b>Remote monitoring</b>			
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  $\leq 55$  mm; left ventricular ejection fraction  $\geq 45\%$ ), 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<sup>2</sup>, 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 thrombosis 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
<b>Device malfunction</b>			
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	
<b>Pump thrombosis</b>			
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*)

<b>Events of bleeding during LT-MCS</b>			
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]
<b>Prevention and treatment of cerebrovascular accidents</b>			
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]
<b>Cardiac arrhythmias</b>			
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
<b>Diagnosis</b>			
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]
<b>Treatment of moderate aortic insufficiency</b>			
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]
<b>Treatment of severe aortic insufficiency</b>			
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
<b>Diagnosis</b>			
Routine follow-up echocardiography for assessment of right heart function is recommended.	I	C	
Invasive haemodynamic measurements should be considered.	IIa	C	[470]
<b>Treatment</b>			
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 anti-fungal 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
<b>Infection prevention prior to LT-MCS implant</b>			
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 <i>Staphylococcus aureus</i> and, if positive, treatment with topical antibiotics prior to LT-MCS device implantation, are recommended.	I	C	[486, 487]
<b>Antibiotic prophylaxis</b>			
Preoperative antimicrobial prophylaxis targeted at <i>Staphylococcus</i> sp. and methicillin-resistant <i>S. aureus</i> (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]
<b>Managing active infection preimplant</b>			
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*)

<b>Infective endocarditis treatment preimplant</b>			
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	
<b>Preventing infection postimplant</b>			
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]
<b>Evaluation of patients with mechanical circulatory support with a suspected infection</b>			
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]
<b>Treatment of patients with mechanical circulatory support with a suspected infection of the driveline exit site or the driveline itself</b>			
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 <i>Staphylococcus</i> , <i>Pseudomonas</i> and <i>Enterobacteriaceae</i> species, also taking local institutional epidemiology and colonization (e.g. methicillin-resistant <i>Staphylococcus aureus</i> , vancomycin-resistant <i>Enterococci</i> ) 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 infectious 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.	<b>IIa</b>	<b>C</b>	[496, 497]
Leucocyte radiolabelled scintigraphy for identification of deep infection may be considered.	<b>IIb</b>	<b>C</b>	[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.	<b>IIa</b>	<b>C</b>	
Lifelong antibiotic treatment for complicated <i>S. aureus</i> infection should be considered unless there is an option to remove the device.	<b>IIa</b>	<b>C</b>	
<b>Treatment of patients with mechanical circulatory support with a suspected infection of the pump</b>			
In all patients with mechanical circulatory support, a full evaluation for any suspected infection as outlined above should be performed before commencing antimicrobial treatment.	<b>I</b>	<b>C</b>	[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.	<b>I</b>	<b>C</b>	
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.	<b>I</b>	<b>C</b>	[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.	<b>IIa</b>	<b>C</b>	

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.	Ila	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.

## REFERENCES

- [1] GHS. German Heart Society. Deutscher Herzbericht 2017 Sektorenübergreifende Versorgungsanalyse zur Kardiologie, Herzchirurgie und Kinderherzmedizin in Deutschland. e.V. DH, Frankfurt am Main, Germany, 2017.
- [2a] Mehra MR, Goldstein DJ, Uriel N, Cleveland JC, Yuzefpolskaya M, Salerno C *et al.* Two-year outcomes with a magnetically levitated cardiac pump in heart failure. *N Engl J Med* 2018;378:1386–95.
- [2b] Morshuis M, Garbade J, Zimpfer D, Shaw S, Lavee J, Gustafsson F *et al.* Clinical outcomes with HeartMate 3TM left ventricular assist device as treatment for advanced heart failure: 12-month outcomes from the ELEVATE Registry. *J Heart Lung Transplant* 2018;37:S84.
- [3] Kirklin JK, Cantor R, Mohacsi P, Gummert J, De By T, Hannan MM *et al.* First annual IMACS report: a global International Society for Heart and Lung Transplantation Registry for mechanical circulatory support. *J Heart Lung Transplant* 2016;35:407–12.
- [4] Baras Shreibati J, Goldhaber-Fiebert JD, Banerjee D, Owens DK, Hlatky MA. Cost-effectiveness of left ventricular assist devices in ambulatory patients with advanced heart failure. *JACC Heart Fail* 2017;5:110–19.
- [5] Rogers JG, Bostic RR, Tong KB, Adamson R, Russo M, Slaughter MS. Cost-effectiveness analysis of continuous-flow left ventricular assist devices as destination therapy. *Circ Heart Fail* 2012;5:10–16.
- [6] Tsiouris A, Paone G, Nemej HW, Brewer RJ, Morgan JA. Factors determining post-operative readmissions after left ventricular assist device implantation. *J Heart Lung Transplant* 2014;33:1041–7.
- [7] Bruce CR, Minard CG, Wilhelms LA, Abraham M, Amione-Guerra J, Pham L *et al.* Caregivers of patients with left ventricular assist devices: possible impacts on patients' mortality and Interagency Registry for Mechanically Assisted Circulatory Support-defined morbidity events. *Circ Cardiovasc Qual Outcomes* 2017;10:1–10.
- [8] Lund LH. Optimizing outcomes after heart transplantation. *Eur J Heart Fail* 2018;20:395–7.
- [9] Ponikowski P, Voors AA, Anker SD, Bueno H, Cleland JG, Coats AJ *et al.* 2016 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure: the Task Force for the diagnosis and treatment of acute and chronic heart failure of the European Society of Cardiology (ESC). Developed with the special contribution of the Heart Failure Association (HFA) of the ESC. *Eur J Heart Fail* 2016;18: 891–975.
- [10] Stevenson LW, Pagani FD, Young JB, Jessup M, Miller L, Kormos RL *et al.* INTERMACS profiles of advanced heart failure: the current picture. *J Heart Lung Transplant* 2009;28:535–41.
- [11] den Uil CA, Akin S, Jewbali LS, Dos Reis Miranda D, Brugts JJ, Constantinescu AA *et al.* Short-term mechanical circulatory support as a bridge to durable left ventricular assist device implantation in refractory cardiogenic shock: a systematic review and meta-analysis. *Eur J Cardiothorac Surg* 2017;52:14–25.
- [12] Shah P, Pagani FD, Desai SS, Rongione AJ, Maltais S, Haglund NA *et al.* Outcomes of patients receiving temporary circulatory support before durable ventricular assist device. *Ann Thorac Surg* 2017;103:106–12.
- [13] Rahimi K, Bennett D, Conrad N, Williams TM, Basu J, Dwight J *et al.* Risk prediction in patients with heart failure: a systematic review and analysis. *JACC Heart Fail* 2014;2:440–6.
- [14] Ouwerkerk W, Voors AA, Zwinderman AH. Factors influencing the predictive power of models for predicting mortality and/or heart failure hospitalization in patients with heart failure. *JACC Heart Fail* 2014;2:429–36.
- [15] Ravichandran AK, Cowger J. Left ventricular assist device patient selection: do risk scores help? *J Thorac Dis* 2015;7:2080–7.
- [16] Lund LH, Stehlik J. Risk scores and biomarkers in heart failure: a journey to predictive accuracy and clinical utility. *J Heart Lung Transplant* 2016; 35:711–13.

- [17] Mehra MR, Canter CE, Hannan MM, Semigran MJ, Uber PA, Baran DA *et al.* The 2016 International Society for Heart Lung Transplantation listing criteria for heart transplantation: a 10-year update. *J Heart Lung Transplant* 2016;35:1–23.
- [18] Braunwald E. Biomarkers in heart failure. *N Engl J Med* 2008;358:2148–59.
- [19] Wright GA, Rauf A, Stoker S, Alharethi R, Kfoury AG. Marital status and survival in left ventricular assist device patient populations. *J Heart Lung Transplant* 2015;34:619–21.
- [20] Cowger JA, Stulak JM, Shah P, Dardas TF, Pagani FD, Dunlay SM *et al.* Impact of center left ventricular assist device volume on outcomes after implantation: an INTERMACS analysis. *JACC Heart Fail* 2017;5:691–9.
- [21] Zabarovskaja S, Gadler F, Gabrielsen A, Linde C, Lund LH. Identifying patients for advanced heart failure therapy by screening patients with cardiac resynchronization therapy or implantable cardioverter-defibrillator: a pilot study. *J Heart Lung Transplant* 2013;32:651–4.
- [22] Pocock SJ, Wang D, Pfeffer MA, Yusuf S, McMurray JJ, Swedberg KB *et al.* Predictors of mortality and morbidity in patients with chronic heart failure. *Eur Heart J* 2006;27:65–75.
- [23] Cotts WG, McGee EC Jr, Myers SL, Naftel DC, Young JB, Kirklin JK *et al.* Predictors of hospital length of stay after implantation of a left ventricular assist device: an analysis of the INTERMACS Registry. *J Heart Lung Transplant* 2014;33:682–8.
- [24] Adamson RM, Stahovich M, Chillcott S, Baradaran S, Chammas J, Jaski B *et al.* Clinical strategies and outcomes in advanced heart failure patients older than 70 years of age receiving the HeartMate II left ventricular assist device: a community hospital experience. *J Am Coll Cardiol* 2011;57:2487–95.
- [25] Kirklin JK, Naftel DC, Pagani FD, Kormos RL, Stevenson LW, Blume ED *et al.* Seventh INTERMACS annual report: 15,000 patients and counting. *J Heart Lung Transplant* 2015;34:1495–504.
- [26] Kusne S, Mooney M, Danziger-Isakov L, Kaan A, Lund LH, Lyster H *et al.* An ISHLT consensus document for prevention and management strategies for mechanical circulatory support infection. *J Heart Lung Transplant* 2017;36:1137–53.
- [27] Sims DB, Uriel N, Gonzalez-Costello J, Deng MC, Restaino SW, Farr MA *et al.* Human immunodeficiency virus infection and left ventricular assist devices: a case series. *J Heart Lung Transplant* 2011;30:1060–4.
- [28] Butler J, Howser R, Portner PM, Pierson RN 3rd. Diabetes and outcomes after left ventricular assist device placement. *J Card Fail* 2005;11:510–15.
- [29] Topkara VK, Dang NC, Martens TP, Cheema FH, Liu JF, Liang LM *et al.* Effect of diabetes on short- and long-term outcomes after left ventricular assist device implantation. *J Heart Lung Transplant* 2005;24:2048–53.
- [30] Uriel N, Naka Y, Colombo PC, Farr M, Pak SW, Cotlarlan V *et al.* Improved diabetic control in advanced heart failure patients treated with left ventricular assist devices. *Eur J Heart Fail* 2011;13:195–9.
- [31] Lofman I, Szummer K, Dahlstrom U, Jernberg T, Lund LH. Associations with and prognostic impact of chronic kidney disease in heart failure with preserved, mid-range, and reduced ejection fraction. *Eur J Heart Fail* 2017;19:1606–14.
- [32] Smith GL, Lichtman JH, Bracken MB, Shlipak MG, Phillips CO, DiCapua P *et al.* Renal impairment and outcomes in heart failure: systematic review and meta-analysis. *J Am Coll Cardiol* 2006;47:1987–96.
- [33] Gustafsson F, Rogers JG. Left ventricular assist device therapy in advanced heart failure: patient selection and outcomes. *Eur J Heart Fail* 2017;19:595–602.
- [34] Topkara VK, Coromilas EJ, Garan AR, Li RC, Castagna F, Jennings DL *et al.* Preoperative proteinuria and reduced glomerular filtration rate predicts renal replacement therapy in patients supported with continuous-flow left ventricular assist devices. *Circ Heart Fail* 2016;9:1–9.
- [35] Klovaite J, Gustafsson F, Mortensen SA, Sander K, Nielsen LB. Severely impaired von Willebrand factor-dependent platelet aggregation in patients with a continuous-flow left ventricular assist device (HeartMate II). *J Am Coll Cardiol* 2009;53:2162–7.
- [36] Starling RC, Moazami N, Silvestry SC, Ewald G, Rogers JG, Milano CA *et al.* Unexpected abrupt increase in left ventricular assist device thrombosis. *N Engl J Med* 2014;370:33–40.
- [37] Slaughter M, Pagani F, Rogers J, Miller LW, Sun B, Russell SD *et al.* Clinical management of continuous-flow left ventricular assist devices in advanced heart failure. *J Heart Lung Transplant* 2010;29:1–39.
- [38] Demirozu ZT, Radovancevic R, Hochman LF, Gregoric ID, Letsou GV, Kar B *et al.* Arteriovenous malformation and gastrointestinal bleeding in patients with the HeartMate II left ventricular assist device. *J Heart Lung Transplant* 2011;30:849–53.
- [39] Holley CT, Fitzpatrick M, Roy SS, Alraies MC, Cogswell R, Souslian L *et al.* Aortic insufficiency in continuous-flow left ventricular assist device support patients is common but does not impact long-term mortality. *J Heart Lung Transplant* 2017;36:91–6.
- [40] Pal JD, Klodell CT, John R, Pagani FD, Rogers JG, Farrar DJ *et al.* Low operative mortality with implantation of a continuous-flow left ventricular assist device and impact of concurrent cardiac procedures. *Circulation* 2009;120:S215–19.
- [41] Yang JA, Kato TS, Shulman BP, Takayama H, Farr M, Jorde UP *et al.* Liver dysfunction as a predictor of outcomes in patients with advanced heart failure requiring ventricular assist device support: use of the Model of End-stage Liver Disease (MELD) and MELD eXcluding INR (MELD-XI) scoring system. *J Heart Lung Transplant* 2012;31:601–10.
- [42] Cermakova P, Lund LH, Fereshtehnejad SM, Johnell K, Winblad B, Dahlstrom U *et al.* Heart failure and dementia: survival in relation to types of heart failure and different dementia disorders. *Eur J Heart Fail* 2015;17:612–19.
- [43] Kato TS, Schulze PC, Yang J, Chan E, Shahzad K, Takayama H *et al.* Preoperative and post-operative risk factors associated with neurologic complications in patients with advanced heart failure supported by a left ventricular assist device. *J Heart Lung Transplant* 2012;31:1–8.
- [44] Flint KM, Matlock DD, Lindenfeld J, Allen LA. Frailty and the selection of patients for destination therapy left ventricular assist device. *Circ Heart Fail* 2012;5:286–93.
- [45] Moayed Y, Duero Posada JG, Foroutan F, Goldraich LA, Alba AC, MacIver J *et al.* The prognostic significance of frailty compared to peak oxygen consumption and B-type natriuretic peptide in patients with advanced heart failure. *Clin Transplant* 2018;32:1–6.
- [46] Jha SR, Ha HS, Hickman LD, Hannu M, Davidson PM, Macdonald PS *et al.* Frailty in advanced heart failure: a systematic review. *Heart Fail Rev* 2015;20:553–60.
- [47] Tse G, Gong M, Wong SH, Wu WKK, Bazoukis G, Lampropoulos K *et al.* Frailty and clinical outcomes in advanced heart failure patients undergoing left ventricular assist device implantation: a systematic review and meta-analysis. *J Am Med Dir Assoc* 2018;19:255–61.e1.
- [48] Dunlay SM, Park SJ, Joyce LD, Daly RC, Stulak JM, McNallan SM *et al.* Frailty and outcomes after implantation of left ventricular assist device as destination therapy. *J Heart Lung Transplant* 2014;33:359–65.
- [49] Reynard AK, Butler RS, McKee MG, Starling RC, Gorodeski EZ. Frequency of depression and anxiety before and after insertion of a continuous flow left ventricular assist device. *Am J Cardiol* 2014;114:433–40.
- [50] Psychosocial Outcomes Workgroup of the Nursing and Social Sciences Council of the International Society for Heart and Lung Transplantation, Cupples S, Dew MA, Grady KL, De Geest S, Dobbels F, *et al.* Report of the Psychosocial Outcomes Workgroup of the Nursing and Social Sciences Council of the International Society for Heart and Lung Transplantation: present status of research on psychosocial outcomes in cardiothoracic transplantation: review and recommendations for the field. *J Heart Lung Transplant* 2006;25:716–25.
- [51] Eshelman AK, Mason S, Neme H, Williams C. LVAD destination therapy: applying what we know about psychiatric evaluation and management from cardiac failure and transplant. *Heart Fail Rev* 2009;14:21–8.
- [52] Kaan A, Young QR, Cockell S, Mackay M. Emotional experiences of caregivers of patients with a ventricular assist device. *Prog Transplant* 2010;20:142–7.
- [53] Bunzel B, Laederach-Hofmann K, Wieselthaler G, Roethy W, Wolner E. Mechanical circulatory support as a bridge to heart transplantation: what remains? Long-term emotional sequelae in patients and spouses. *J Heart Lung Transplant* 2007;26:384–9.
- [54] Lund LH, Matthews J, Aaronson K. Patient selection for left ventricular assist devices. *Eur J Heart Fail* 2010;12:434–43.
- [55] Schibilsky D, Haller C, Lange B, Schibilsky B, Haeberle H, Seizer P *et al.* Extracorporeal life support prior to left ventricular assist device implantation leads to improvement of the patients INTERMACS levels and outcome. *PLoS One* 2017;12:1–9.
- [56] Kirklin JK, Naftel DC, Kormos RL, Pagani FD, Myers SL, Stevenson LW *et al.* Quantifying the effect of cardiorenal syndrome on mortality after left ventricular assist device implant. *J Heart Lung Transplant* 2013;32:1205–13.
- [57] Kim JH, Singh R, Pagani FD, Desai SS, Haglund NA, Dunlay SM *et al.* Ventricular assist device therapy in older patients with heart failure: characteristics and outcomes. *J Card Fail* 2016;22:981–7.
- [58] Patil NP, Mohite PN, Sabashnikov A, Dhar D, Weymann A, Zeriyoh M *et al.* Preoperative predictors and outcomes of right ventricular assist

- device implantation after continuous-flow left ventricular assist device implantation. *J Thorac Cardiovasc Surg* 2015;150:1651-8.
- [59] Maltais S, Stulak JM. Right and left ventricular assist devices support and liver dysfunction: prognostic and therapeutic implications. *Curr Opin Cardiol* 2016;31:287-91.
- [60] Pappalardo F, Regazzoli D, Mangieri A, Ajello S, Melisurgo G, Agricola E *et al.* Hemodynamic and echocardiographic effects of aortic regurgitation on femoro-femoral veno-arterial ECMO. *Int J Cardiol* 2016;202:760-2.
- [61] Boulate D, Luyt CE, Pozzi M, Niculescu M, Combes A, Leprince P *et al.* Acute lung injury after mechanical circulatory support implantation in patients on extracorporeal life support: an unrecognized problem. *Eur J Cardiothorac Surg* 2013;44:544-9; discussion 49-50.
- [62] Pappalardo F, Schulte C, Pieri M, Schrage B, Contri R, Soeffker G *et al.* Concomitant implantation of Impella(R) on top of veno-arterial extracorporeal membrane oxygenation may improve survival of patients with cardiogenic shock. *Eur J Heart Fail* 2017;19:404-12.
- [63] Matthews JC, Pagani FD, Haft JW, Koelling TM, Naftel DC, Aaronson KD. Model for end-stage liver disease score predicts left ventricular assist device operative transfusion requirements, morbidity, and mortality. *Circulation* 2010;121:214-20.
- [64] Pagano D, Milojevic M, Meesters MI, Benedetto U, Bolliger D, von Heymann C *et al.* 2017 EACTS/EACTA Guidelines on patient blood management for adult cardiac surgery. *Eur J Cardiothorac Surg* 2018;53:79-111.
- [65] Dang NC, Topkara VK, Kim BT, Lee BJ, Remoli R, Naka Y. Nutritional status in patients on left ventricular assist device support. *J Thorac Cardiovasc Surg* 2005;130:e3-4.
- [66] Holdy K, Dembitsky W, Eaton LL, Chillcott S, Stahovich M, Rasmuson B *et al.* Nutrition assessment and management of left ventricular assist device patients. *J Heart Lung Transplant* 2005;24:1690-6.
- [67] Kirklin JK, Pagani FD, Kormos RL, Stevenson LW, Blume ED, Myers SL *et al.* Eighth annual INTERMACS report: special focus on framing the impact of adverse events. *J Heart Lung Transplant* 2017;36:1080-6.
- [68] Jorde UP, Uriel N, Nahumi N, Bejar D, Gonzalez-Costello J, Thomas SS *et al.* Prevalence, significance, and management of aortic insufficiency in continuous flow left ventricular assist device recipients. *Circ Heart Fail* 2014;7:310-19.
- [69] Robertson JO, Naftel DC, Myers SL, Prasad S, Mertz GD, Itoh A *et al.* Concomitant aortic valve procedures in patients undergoing implantation of continuous-flow left ventricular assist devices: an INTERMACS database analysis. *J Heart Lung Transplant* 2015;34:797-805.
- [70] Fukuhara S, Ikegami H, Polanco AR, Song JJ, Han J, Takeda K *et al.* Concomitant repair for mild aortic insufficiency and continuous-flow left ventricular assist devices. *Eur J Cardiothorac Surg* 2017;52:1062-8.
- [71] Feldman D, Pamboukian SV, Teuteberg JJ, Birks E, Lietz K, Moore SA *et al.* The 2013 International Society for Heart and Lung Transplantation Guidelines for mechanical circulatory support: executive summary. *J Heart Lung Transplant* 2013;32:157-87.
- [72] Stainback RF, Estep JD, Agler DA, Birks EJ, Bremer M, Hung J *et al.* Echocardiography in the management of patients with left ventricular assist devices: recommendations from the American Society of Echocardiography. *J Am Soc Echocardiogr* 2015;28:853-909.
- [73] Tanaka A, Onsager D, Song T, Cozadd D, Kim G, Sarswat N *et al.* Surgically corrected mitral regurgitation during left ventricular assist device implantation is associated with low recurrence rate and improved midterm survival. *Ann Thorac Surg* 2017;103:725-33.
- [74] Sandoval E, Singh SK, Carillo JA, Baldwin ACW, Ono M, Anand J *et al.* Impact of concomitant mitral valve repair for severe mitral regurgitation at the time of continuous-flow left ventricular assist device insertion. *Interact CardioVasc Thorac Surg* 2017;25:620-3.
- [75] Robertson JO, Naftel DC, Myers SL, Tedford RJ, Joseph SM, Kirklin JK *et al.* Concomitant mitral valve procedures in patients undergoing implantation of continuous-flow left ventricular assist devices: an INTERMACS database analysis. *J Heart Lung Transplant* 2018;37:79-88.
- [76] Dandel M, Krabatsch T, Falk V. Left ventricular vs. biventricular mechanical support: decision-making and strategies for avoidance of right heart failure after left ventricular assist device implantation. *Int J Cardiol* 2015;198:241-50.
- [77] Brewer RJ, Cabrera R, El-Atrache M, Zafar A, Hrobowski TN, Nemeš HM *et al.* Relationship of tricuspid repair at the time of left ventricular assist device implantation and survival. *Int J Artif Organs* 2014;37:834-8.
- [78] Robertson JO, Grau-Sepulveda MV, Okada S, O'Brien SM, Matthew Brennan J, Shah AS *et al.* Concomitant tricuspid valve surgery during implantation of continuous-flow left ventricular assist devices: a Society of Thoracic Surgeons database analysis. *J Heart Lung Transplant* 2014;33:609-17.
- [79] Kirchhof P, Benussi S, Kotecha D, Ahlsson A, Atar D, Casadei B *et al.* 2016 ESC Guidelines for the management of atrial fibrillation developed in collaboration with EACTS. *Eur J Cardiothorac Surg* 2016;50:e1-e88.
- [80] Song HK, Gelow JM, Mudd J, Chien C, Tibayan FA, Hollifield K *et al.* Limited utility of tricuspid valve repair at the time of left ventricular assist device implantation. *Ann Thorac Surg* 2016;101:2168-74.
- [81] Bartfay S-E, Dellgren G, Lidén H, Holmberg M, Gäbel J, Redfors B *et al.* Are biventricular assist devices underused as a bridge to heart transplantation in patients with a high risk of postimplant right ventricular failure? *J Thorac Cardiovasc Surg* 2017;153:360-7.e1.
- [82] Maury P, Delmas C, Trouillet C, Slaughter MS, Lairez O, Galinier M *et al.* First experience of percutaneous radio-frequency ablation for atrial flutter and atrial fibrillation in a patient with HeartMate II left ventricular assist device. *J Interv Card Electrophysiol* 2010;29:63-7.
- [83] Calkins H, Hindricks G, Cappato R, Kim Y-H, Saad EB, Aguinaga L *et al.* 2017 HRS/EHRA/ECAS/APHRS/SOLAECE expert consensus statement on catheter and surgical ablation of atrial fibrillation: executive summary. *Heart Rhythm* 2017;14:e445-94.
- [84] Clerkin KJ, Topkara VK, Demmer RT, Dizon JM, Yuzefpolskaya M, Fried JA *et al.* Implantable cardioverter-defibrillators in patients with a continuous-flow left ventricular assist device: an analysis of the INTERMACS Registry. *JACC Heart Fail* 2017;5:916-26.
- [85] Boudghene-Stambouli F, Boule S, Goeminne C, Botcherby E, Marquie C, Kouakam C *et al.* Clinical implications of left ventricular assist device implantation in patients with an implantable cardioverter-defibrillator. *J Interv Card Electrophysiol* 2014;39:177-84.
- [86] Mulloy DP, Bhamidipati CM, Stone ML, Ailawadi G, Bergin JD, Mahapatra S *et al.* Cryoablation during left ventricular assist device implantation reduces postoperative ventricular tachyarrhythmias. *J Thorac Cardiovasc Surg* 2013;145:1207-13.
- [87] Patel M, Rojas F, Shabari FR, Simpson L, Cohn W, Frazier OH *et al.* Safety and feasibility of open chest epicardial mapping and ablation of ventricular tachycardia during the period of left ventricular assist device implantation. *J Cardiovasc Electrophysiol* 2016;27:95-101.
- [88] Friedman DJ, Piccini JP, Wang T, Zheng J, Malaisrie SC, Holmes DR *et al.* Association between left atrial ablation during and readmission for thromboembolism among patients with atrial fibrillation undergoing concomitant cardiac surgery. *JAMA* 2018;319:365-74.
- [89] Ozbaran M, Yagdi T, Engin C, Nalbantgil S, Ertugay S, Ozturk P. Left ventricular assist device implantation by lateral thoracotomy to the descending aorta: a propensity matched analysis to standard sternotomy approach. *J Heart Lung Transplant* 2016;35:3522.
- [90] Chou J, Bermudez C, Kormos R, Teuteberg J. Permanent continuous flow left ventricular assist devices use after acute stabilization for cardiogenic shock in acute myocardial infarction. *ASAIO J* 2017;63:e13-17.
- [91] De By TMMH, Mohacsi P, Gahl B, Zittermann A, Krabatsch T, Gustafsson F *et al.* The European Registry for Patients with Mechanical Circulatory Support (EUROMACS) of the European Association for Cardio-Thoracic Surgery (EACTS): second report. *Eur J Cardiothorac Surg* 2018;53:309-16.
- [92] Kirklin JK, Xie R, Cowger J, de By T, Nakatani T, Schueler S *et al.* Second annual report from the ISHLT Mechanically Assisted Circulatory Support Registry. *J Heart Lung Transplant* 2018;37:685-91.
- [93] Sigurdardottir V, Bjortuft O, Eiskjær H, Ekmehag B, Gude E, Gustafsson F *et al.* Long-term follow-up of lung and heart transplant recipients with pre-transplant malignancies. *J Heart Lung Transplant* 2012;31:1276-80.
- [94] Joyce E. Frailty in advanced heart failure. *Heart Fail Clin* 2016;12:363-74.
- [95] Cooper LB, Hammill BG, Allen LA, Lindenfeld J, Mentz RJ, Rogers JG *et al.* Assessing frailty in patients undergoing destination therapy left ventricular assist device: observations from Interagency Registry for Mechanically Assisted Circulatory Support. *ASAIO J* 2018;64:16-23.
- [96] Joseph SM, Manghelli JL, Vader JM, Keeney T, Novak EL, Felius J *et al.* Prospective assessment of frailty using the fried criteria in patients undergoing left ventricular assist device therapy. *Am J Cardiol* 2017;120:1349-54.
- [97] Maurer MS, Horn E, Reyentovich A, Dickson VV, Pinney S, Goldwater D *et al.* Can a left ventricular assist device in individuals with advanced systolic heart failure improve or reverse frailty? *J Am Geriatr Soc* 2017;65:2383-90.
- [98] Lushaj EB, Badami A, Osaki S, Murray M, Levenson G, Lozonschi L *et al.* Impact of age on outcomes following continuous-flow left ventricular assist device implantation. *Interact CardioVasc Thorac Surg* 2015;20:743-8.

- [99] Morgan J, Neme H, Paone G. Should left ventricular assist devices be implanted in patients seventy years of age and older: a comparative analysis. *Heart Surg Forum* 2014;17:182–6.
- [100] Loncar G, Springer J, Anker M, Doehner W, Lainscak M. Cardiac cachexia: hic et nunc. *J Cachexia Sarcopenia Muscle* 2016;7:246–60.
- [101] Flint KM, Matlock DD, Sundareswaran KS, Lindenfeld J, Spertus JA, Farrar DJ *et al.* Pre-operative health status and outcomes after continuous-flow left ventricular assist device implantation. *J Heart Lung Transplant* 2013;32:1249–54.
- [102] Yost G, Tatoes A, Bhat G. Preoperative nutritional assessment with the prognostic nutrition index in patients undergoing left ventricular assist device implantation. *ASAIO J* 2018;64:52–5.
- [103] Patel AM, Adeseun G, Ahmed I, Mitter N, Rame JE, Rudnick MR. Renal failure in patients with left ventricular assist devices. *Clin J Am Soc Nephrol* 2013;8:484–96.
- [104] Bhat G, Yost G, Mahoney E. Cognitive function and left ventricular assist device implantation. *J Heart Lung Transplant* 2015;34:1398–405.
- [105] Maldonado JR, Sher Y, Lolak S, Swendsen H, Skibola D, Neri E *et al.* The Stanford Integrated Psychosocial Assessment for Transplantation: a prospective study of medical and psychosocial outcomes. *Psychosom Med* 2015;77:1018–30.
- [106] Vandenberg E, Doering L, Chen B, Saltzman A, Chaker T, Creaser JW *et al.* Evaluation of the SIPAT instrument to assess psychosocial risk in heart transplant candidates: a retrospective single center study. *Heart Lung* 2017;46:273–9.
- [107] Mikus E, Stepanenko A, Krabatsch T, Dandel M, Lehmkühl HB, Loforte A *et al.* Left ventricular assist device or heart transplantation: impact of transpulmonary gradient and pulmonary vascular resistance on decision-making. *Eur J Cardiothorac Surg* 2011;39:310–16.
- [108] Beyersdorf F, Schlensak C, Berchtold-Herz M, Trummer G. Regression of “fixed” pulmonary vascular resistance in heart transplant candidates after unloading with ventricular assist devices. *J Thorac Cardiovasc Surg* 2010;140:747–9.
- [109] Salzberg SP, Lachat ML, von Harbou K, Zünd G, Turina MI. Normalization of high pulmonary vascular resistance with LVAD support in heart transplantation candidates. *Eur J Cardiothorac Surg* 2005;27:222–5.
- [110] Stathatos N, Wartofsky L. The euthyroid sick syndrome: is there a physiologic rationale for thyroid hormone treatment? *J Endocrinol Invest* 2003;26:1174–9.
- [111] Carrel T, Eckstein F, Englberger L, Mury R, Mohacsi P. Thyronin treatment in adult and pediatric heart surgery: clinical experience and review of the literature. *Eur J Heart Fail* 2002;4:577–82.
- [112] Vest A, Mistak S, Hachamovitch R. Outcomes for patients with diabetes after continuous-flow left ventricular assist device implantation. *J Card Fail* 2016;22:780–996.
- [113] Mohamedali B, Yost G, Bhat G. Is diabetes mellitus a risk factor for poor prognosis after left ventricular assist device placement? *Tex Heart Inst J* 2017;44:115–19.
- [114] Mohamedali B, Yost G, Bhat G. Mechanical circulatory support improves diabetic control in patients with advanced heart failure. *Eur J Heart Fail* 2014;16:1120–4.
- [115] van den Berge JC, Constantinescu AA, Boiten HJ, van Domburg RT, Deckers JW, Akkerhuis KM. Short- and long-term prognosis of patients with acute heart failure with and without diabetes: changes over the last three decades. *Diabetes Care* 2018;41:143–9.
- [116] Bhat G, Gopalakrishnan M, Aggarwal A. Gastrointestinal bleeding with continuous flow left ventricular assist devices (LVADs). In: Komamura K (ed). *Cardiology and Cardiovascular Medicine: Recent Advances in the Field of Ventricular Assist Devices*. IntechOpen Limited, London, pp. 51–66. 2013.
- [117] Uriel N, Pak S-W, Jorde UP, Jude B, Susen S, Vincentelli A *et al.* Acquired von Willebrand syndrome after continuous-flow mechanical device support contributes to a high prevalence of bleeding during long-term support and at the time of transplantation. *J Am Coll Cardiol* 2010;56:1207–13.
- [118] Mohacsi P, Meier B. Hypoxic hepatitis in patients with cardiac failure. *J Hepatol* 1994;21:693–5.
- [119] Gelow JM, Desai AS, Hochberg CP, Glickman JN, Givertz MM, Fang JC. Clinical predictors of hepatic fibrosis in chronic advanced heart failure. *Circ Heart Fail* 2010;3:59–64.
- [120] Modi A, Vohra H, Barlow C. Do patients with liver cirrhosis undergoing cardiac surgery have acceptable outcomes? *Interact CardioVasc Thorac Surg* 2010;11:630–4.
- [121] Potthoff A, Schettler A, Attia D, Schlue J, Schmitto JD, Fegbeutel C *et al.* Liver stiffness measurements and short-term survival after left ventricular assist device implantation: a pilot study. *J Heart Lung Transplant* 2015;34:1586–94.
- [122] Demirozu ZT, Hernandez R, Mallidi HR, Singh SK, Radovancevic R, Segura AM *et al.* HeartMate II left ventricular assist device implantation in patients with advanced hepatic dysfunction. *J Card Surg* 2014;29:419–23.
- [123] Amione-Guerra J, Cruz-Solbes AS, Gonzalez Bonilla H, Estep JD, Guha A, Bhimaraj A *et al.* Melding a high-risk patient for continuous flow left ventricular assist device into a low-risk patient. *ASAIO J* 2017;63:704–12.
- [124] Deo SV, Daly RC, Altarabsheh SE, Hasin T, Zhao Y, Shah IK *et al.* Predictive value of the model for end-stage liver disease score in patients undergoing left ventricular assist device implantation. *ASAIO J* 2013;59:57–62.
- [125] Nishi H, Toda K, Miyagawa S, Yoshikawa Y, Fukushima S, Yoshioka D *et al.* Prediction of outcome in patients with liver dysfunction after left ventricular assist device implantation. *J Artif Organs* 2013;16:404–10.
- [126] Weymann A, Patil NP, Sabashnikov A, Mohite PN, Garcia Saez D, Bireta C *et al.* Continuous-flow left ventricular assist device therapy in patients with preoperative hepatic failure: are we pushing the limits too far? *Artif Organs* 2015;39:336–42.
- [127] Woolley JR, Kormos RL, Teuteberg JJ, Bermudez CA, Bhama JK, Lockard KL *et al.* Preoperative liver dysfunction influences blood product administration and alterations in circulating haemostatic markers following ventricular assist device implantation. *Eur J Cardiothorac Surg* 2015;47:497–504.
- [128] Lueck S, Sindermann J, Martens S, Scherer M. Mechanical circulatory support for patients with peripartum cardiomyopathy. *J Artif Organs* 2016;19:305–9.
- [129] Makdisi G, Jan MY, Dungy-Poythress L, Wang IW, Caccamo MA. Successful delivery in a patient with left ventricular assist device and unplanned pregnancy. *Ann Thorac Surg* 2017;104:e31–3.
- [130] Zimpfer D, Zrunek P, Roethy W, Czerny M, Schima H, Huber L *et al.* Left ventricular assist devices decrease fixed pulmonary hypertension in cardiac transplant candidates. *J Thorac Cardiovasc Surg* 2007;133:689–95.
- [131] Mikus E, Stepanenko A, Krabatsch T, Loforte A, Dandel M, Lehmkühl HB. Reversibility of fixed pulmonary hypertension in left ventricular assist device support recipients. *Eur J Cardiothorac Surg* 2011;40:971–7.
- [132] Fendler TJ, Spertus JA, Gosch KL, Jones PG, Bruce JM, Nassif ME *et al.* Incidence and predictors of cognitive decline in patients with left ventricular assist devices. *Circ Cardiovasc Qual Outcomes* 2015;8:285–91.
- [133] Iodice F, Testa G, Averardi M, Brancaccio G, Amodeo A, Cogo P. Implantation of a left ventricular assist device as a destination therapy in Duchenne muscular dystrophy patients with end stage cardiac failure: management and lessons learned. *Neuromuscular Disord* 2015;25:19–23.
- [134] Cajita MI, Baumgartner E, Berben L, Denhaerynck K, Helmy R, Schönfeld S *et al.* Heart transplant centers with multidisciplinary team show a higher level of chronic illness management—findings from the International BRIGHT Study. *Heart Lung* 2017;46:351–6.
- [135] Fried J, Levin AP, Mody KM, Garan AR, Yuzefpolsakaya M, Takayama H *et al.* Prior hematologic conditions carry a high morbidity and mortality in patients supported with continuous-flow left ventricular assist devices. *J Heart Lung Transplant* 2014;33:1119–25.
- [136] Schroder JN, Daneshmand MA, Villamizar NR, Petersen RP, Blue LJ, Welsby IJ *et al.* Heparin-induced thrombocytopenia in left ventricular assist device bridge-to-transplant patients. *Ann Thorac Surg* 2007;84:841–6.
- [137] Mountis S, Starling R. Management of left ventricular assist devices after surgery: bridge, destination, and recovery. *Curr Opin Cardiol* 2009;24:252–6.
- [138] Starling RC, Naka Y, Boyle AJ, Gonzalez-Stawinski G, John R, Jorde U *et al.* Results of the post-U.S. Food and Drug Administration-approval study with a continuous flow left ventricular assist device as a bridge to heart transplantation: a prospective study using the INTERMACS (Interagency Registry for Mechanically Assisted Circulatory Support). *J Am Coll Cardiol* 2011;57:1890–8.
- [139] Pagani FD, Miller LW, Russell SD, Aaronson KD, John R, Boyle AJ *et al.* Extended mechanical circulatory support with a continuous-flow rotary left ventricular assist device. *J Am Coll Cardiol* 2009;54:312–21.
- [140] Miller LW, Pagani FD, Russell SD, John R, Boyle AJ, Aaronson KD *et al.* Use of a continuous-flow device in patients awaiting heart transplantation. *N Engl J Med* 2007;357:885–96.



- [141] Aaronson KD, Slaughter MS, Miller LW, McGee EC, Cotts WG, Acker MA *et al.* Use of an intrapericardial, continuous-flow, centrifugal pump in patients awaiting heart transplantation. *Circulation* 2012;125:3191–200.
- [142] Slaughter MS, Pagani FD, McGee EC, Birks EJ, Cotts WG, Gregoric I *et al.* HeartWare ventricular assist system for bridge to transplant: combined results of the bridge to transplant and continued access protocol trial. *J Heart Lung Transplant* 2013;32:675–83.
- [143] Strueber M, O'Driscoll G, Jansz P, Khaghani A, Levy WC, Wieselthaler GM. Multicenter evaluation of an intrapericardial left ventricular assist system. *J Am Coll Cardiol* 2011;57:1375–82.
- [144] Krabatsch T, Netuka I, Schmitto JD, Zimpfer D, Garbade J, Rao V *et al.* Heartmate 3 fully magnetically levitated left ventricular assist device for the treatment of advanced heart failure—1 year results from the CE mark trial. *J Cardiothorac Surg* 2017;12:23.
- [145] Mehra MR, Naka Y, Uriel N, Goldstein DJ, Cleveland JC Jr, Colombo PC *et al.* A fully magnetically levitated circulatory pump for advanced heart failure. *N Engl J Med* 2017;376:440–50.
- [146] Rogers JG, Pagani FD, Tatooles AJ, Bhat G, Slaughter MS, Birks EJ *et al.* Intrapericardial left ventricular assist device for advanced heart failure. *N Engl J Med* 2017;376:451–60.
- [147] Slaughter MS, Rogers JG, Milano CA, Russell SD, Conte JV, Feldman D *et al.* Advanced heart failure treated with continuous-flow left ventricular assist device. *N Engl J Med* 2009;361:2241–51.
- [148] Park SJ, Milano CA, Tatooles AJ, Rogers JG, Adamson RM, Steidley DE *et al.* Outcomes in advanced heart failure patients with left ventricular assist devices for destination therapy. *Circ Heart Fail* 2012;5:241–8.
- [149] Jorde UP, Kushwaha SS, Tatooles AJ, Naka Y, Bhat G, Long JW *et al.* Results of the destination therapy post-food and drug administration approval study with a continuous flow left ventricular assist device: a prospective study using the INTERMACS Registry (Interagency Registry for Mechanically Assisted Circulatory Support). *J Am Coll Cardiol* 2014;63:1751–7.
- [150] Gustafsson F, Shaw S, Lavee J, Saeed D, Pya Y, Krabatsch T *et al.* Six-month outcomes after treatment of advanced heart failure with a full magnetically levitated continuous flow left ventricular assist device: report from the ELEVATE registry. *Eur Heart J* 2018;39:3454–60.
- [151] Maltais S, Anwer LA, Tchanchaleishvili V, Haglund NA, Dunlay SM, Aaronson KD *et al.* Left lateral thoracotomy for centrifugal continuous-flow left ventricular assist device placement: an analysis from the mechanical circulatory support research network. *ASAIO J* 2017;64:715–20.
- [152] Sileshi B, O'Hara BK, Davis ME, Haglund NA, Meng X, Deegan R *et al.* Outcomes of patients implanted using a left thoracotomy technique for a miniaturized centrifugal continuous-flow pump. *ASAIO J* 2016;62:539–44.
- [153] Haberl T, Riebandt J, Mahr S, Laufer G, Rajek A, Schima H *et al.* Viennese approach to minimize the invasiveness of ventricular assist device implantation. *Eur J Cardiothorac Surg* 2014;46:991–6; discussion 96.
- [154] Strueber M, Meyer AL, Feussner M, Ender J, Correia JC, Mohr FW. A minimally invasive off-pump implantation technique for continuous-flow left ventricular assist devices: early experience. *J Heart Lung Transplant* 2014;33:851–6.
- [155] Theiss HD, Grabmaier U, Kreissl N, Hagl C, Steinbeck G, Sodiani R *et al.* Preconditioning with levosimendan before implantation of left ventricular assist devices. *Artif Organs* 2014;38:231–4.
- [156] Sponga S, Ivanitskaia E, Potapov E, Krabatsch T, Hetzer R, Lehmkuhl H. Preoperative treatment with levosimendan in candidates for mechanical circulatory support. *ASAIO J* 2012;58:6–11.
- [157] Dandel M, Potapov E, Krabatsch T, Stepanenko A, Low A, Vierecke J *et al.* Load dependency of right ventricular performance is a major factor to be considered in decision-making before ventricular assist device implantation. *Circulation* 2013;128:514–23.
- [158] Kukucka M, Potapov E, Stepanenko A, Weller K, Mladenow A, Kuppe H *et al.* Acute impact of left ventricular unloading by left ventricular assist device on the right ventricle geometry and function: effect of nitric oxide inhalation. *J Thorac Cardiovasc Surg* 2011;141:1009–14.
- [159] Potapov EV, Stepanenko A, Dandel M, Kukucka M, Lehmkuhl HB, Weng Y *et al.* Tricuspid incompetence and geometry of the right ventricle as predictors of right ventricular function after implantation of a left ventricular assist device. *J Heart Lung Transplant* 2008;27:1275–81.
- [160] Raina A, Seetha Rammohan HR, Gertz ZM, Rame JE, Woo YJ, Kirkpatrick JN. Postoperative right ventricular failure after left ventricular assist device placement is predicted by preoperative echocardiographic structural, hemodynamic, and functional parameters. *J Card Fail* 2013;19:16–24.
- [161] Grant AD, Smedira NG, Starling RC, Marwick TH. Independent and incremental role of quantitative right ventricular evaluation for the prediction of right ventricular failure after left ventricular assist device implantation. *J Am Coll Cardiol* 2012;60:521–8.
- [162] Dang NC, Topkara VK, Mercado M, Kay J, Kruger KH, Aboodi MS *et al.* Right heart failure after left ventricular assist device implantation in patients with chronic congestive heart failure. *J Heart Lung Transplant* 2006;25:1–6.
- [163] Matthews JC, Koelling TM, Pagani FD, Aaronson KD. The right ventricular failure risk score a pre-operative tool for assessing the risk of right ventricular failure in left ventricular assist device candidates. *J Am Coll Cardiol* 2008;51:2163–72.
- [164] Ochiai Y, McCarthy PM, Smedira NG, Banbury MK, Navia JL, Feng J *et al.* Predictors of severe right ventricular failure after implantable left ventricular assist device insertion: analysis of 245 patients. *Circulation* 2002;106:1198–202.
- [165] Shiga T, Kinugawa K, Imamura T, Kato N, Endo M, Inaba T *et al.* Combination evaluation of preoperative risk indices predicts requirement of biventricular assist device. *Circ J* 2012;76:2785–91.
- [166] Cleveland JC Jr, Naftel DC, Reece TB, Murray M, Antaki J, Pagani FD *et al.* Survival after biventricular assist device implantation: an analysis of the Interagency Registry for Mechanically Assisted Circulatory Support database. *J Heart Lung Transplant* 2011;30:862–9.
- [167] Takeda K, Naka Y, Yang JA, Uriel N, Colombo PC, Jorde UP *et al.* Timing of temporary right ventricular assist device insertion for severe right heart failure after left ventricular assist device implantation. *ASAIO J* 2013;59:564–9.
- [168] Lazar JF, Swartz MF, Schiralli MP, Schneider M, Pisula B, Hallinan W *et al.* Survival after left ventricular assist device with and without temporary right ventricular support. *Ann Thorac Surg* 2013;96:2155–9.
- [169] Fitzpatrick JR 3rd, Frederick JR, Hiesinger W, Hsu VM, McCormick RC, Kozin ED *et al.* Early planned institution of biventricular mechanical circulatory support results in improved outcomes compared with delayed conversion of a left ventricular assist device to a biventricular assist device. *J Thorac Cardiovasc Surg* 2009;137:971–7.
- [170] Aissaoui N, Morshuis M, Paluszkiwicz L, Lauenroth V, Borgermann J, Gummert J. Comparison of biventricular and left ventricular assist devices for the management of severe right ventricular dysfunction in patients with end-stage heart failure. *ASAIO J* 2014;60:400–6.
- [171] Morgan JA, John R, Lee BJ, Oz MC, Naka Y. Is severe right ventricular failure in left ventricular assist device recipients a risk factor for unsuccessful bridging to transplant and post-transplant mortality. *Ann Thorac Surg* 2004;77:859–63.
- [172] Grimm JC, Sciortino CM, Magruder JT, Dungan SP, Valero V 3rd, Sharma K *et al.* Outcomes in patients bridged with univentricular and biventricular devices in the modern era of heart transplantation. *Ann Thorac Surg* 2016;102:102–8.
- [173] Levin AP, Jaramillo N, Garan AR, Takeda K, Takayama H, Yuzefpolskaya M *et al.* Outcomes of contemporary mechanical circulatory support device configurations in patients with severe biventricular failure. *J Thorac Cardiovasc Surg* 2016;151:530–5.e2.
- [174] Maeder MT, Leet A, Ross A, Esmore D, Kaye DM. Changes in right ventricular function during continuous-flow left ventricular assist device support [corrected]. *J Heart Lung Transplant* 2009;28:360–6.
- [175] Drakos SG, Janicki L, Horne BD, Kfoury AG, Reid BB, Clayton S *et al.* Risk factors predictive of right ventricular failure after left ventricular assist device implantation. *Am J Cardiol* 2010;105:1030–5.
- [176] Kirklin JK, Naftel DC, Kormos RL, Stevenson LW, Pagani FD, Miller MA *et al.* Fifth INTERMACS annual report: risk factor analysis from more than 6,000 mechanical circulatory support patients. *J Heart Lung Transplant* 2013;32:141–56.
- [177] Kormos RL, Teuteberg JJ, Pagani FD, Russell SD, John R, Miller LW *et al.* Right ventricular failure in patients with the HeartMate II continuous-flow left ventricular assist device: incidence, risk factors, and effect on outcomes. *J Thorac Cardiovasc Surg* 2010;139:1316–24.
- [178] Noly PE, Kirsch M, Quessard A, Leger P, Pavie A, Amour J *et al.* Temporary right ventricular support following left ventricle assist device implantation: a comparison of two techniques. *Interact CardioVasc Thorac Surg* 2014;19:49–55.
- [179] Takeda K, Naka Y, Yang JA, Uriel N, Colombo PC, Jorde UP *et al.* Outcome of unplanned right ventricular assist device support for severe right heart failure after implantable left ventricular assist device insertion. *J Heart Lung Transplant* 2014;33:141–8.

- [180] Loforte A, Montalto A, Lilla Della Monica P, Musumeci F. Simultaneous temporary CentriMag right ventricular assist device placement in HeartMate II left ventricular assist system recipients at high risk of right ventricular failure. *Interact CardioVasc Thorac Surg* 2010;10:847–50.
- [181] Takayama H, Naka Y, Kodali SK, Vincent JA, Addonizio LJ, Jorde UP *et al.* A novel approach to percutaneous right-ventricular mechanical support. *Eur J Cardiothorac Surg* 2012;41:423–6.
- [182] Schmack B, Weymann A, Popov AF, Patil NP, Sabashnikov A, Kremer J *et al.* Concurrent left ventricular assist device (LVAD) implantation and percutaneous temporary RVAD support via CardiacAssist Protek-Duo TandemHeart to preempt right heart failure. *Med Sci Monit Basic Res* 2016;22:53–7.
- [183] Schaefer A, Reichart D, Bernhardt AM, Kubik M, Barten MJ, Wagner FM *et al.* Outcomes of minimally invasive temporary right ventricular assist device support for acute right ventricular failure during minimally invasive left ventricular assist device implantation. *ASAIO J* 2017; 63:546–50.
- [184] Saeed D, Maxhera B, Kamiya H, Lichtenberg A, Albert A. Alternative right ventricular assist device implantation technique for patients with perioperative right ventricular failure. *J Thorac Cardiovasc Surg* 2015; 149:927–32.
- [185] Saito S, Sakaguchi T, Miyagawa S, Nishi H, Yoshikawa Y, Fukushima S *et al.* Recovery of right heart function with temporary right ventricular assist using a centrifugal pump in patients with severe biventricular failure. *J Heart Lung Transplant* 2012;31:858–64.
- [186] Loforte A, Stepanenko A, Potapov EV, Musumeci F, Dranishnikov N, Schweiger M *et al.* Temporary right ventricular mechanical support in high-risk left ventricular assist device recipients versus permanent biventricular or total artificial heart support. *Artif Organs* 2013;37:523–30.
- [187] Cheng A, Trivedi JR, Van Berkel VH, Massey HT, Slaughter MS. Comparison of total artificial heart and biventricular assist device support as bridge-to-transplantation. *J Card Surg* 2016;31:648–53.
- [188] Schmack B, Weymann A, Ruschitzka F, Autschbach R, Raake PW, Jurrmann N *et al.* Successful support of biventricular heart failure patients by new EXCOR<sup>®</sup> Adult pumps with bileaflet valves: a prospective study. *Clin Res Cardiol* 2018;107:413–20.
- [189] Tsukui H, Teuteberg JJ, Murali S, McNamara DM, Buchanan JR, Winowich S *et al.* Biventricular assist device utilization for patients with morbid congestive heart failure: a justifiable strategy. *Circulation* 2005; 112:165–72.
- [190] Slaughter MS, Tsui SS, El-Banayosy A, Sun BC, Kormos RL, Mueller DK *et al.* Results of a multicenter clinical trial with the thoratec implantable ventricular assist device. *J Thorac Cardiovasc Surg* 2007;133:1573–80.
- [191] Holman WL, Kormos RL, Naftel DC, Miller MA, Pagani FD, Blume E *et al.* Predictors of death and transplant in patients with a mechanical circulatory support device: a multi-institutional study. *J Heart Lung Transplant* 2009;28:44–50.
- [192] Arabia FA, Milano CA, Mahr C, McGee EC Jr, Mokadam NA, Rame JE *et al.* Biventricular support with intracorporeal, continuous flow, centrifugal ventricular assist devices. *Ann Thorac Surg* 2017;105:548–55.
- [193] Kirsch M, Mazzucotelli JP, Roussel JC, Bouchot O, N'Loga J, Leprince P *et al.* Survival after biventricular mechanical circulatory support: does the type of device matter? *J Heart Lung Transplant* 2012;31:501–8.
- [194] Potapov E, Schweiger M, Vierecke J, Dandel M, Stepanenko A, Kukucka M *et al.* Discontinuation of HeartWare RVAD support without device removal in chronic BIVAD patients. *ASAIO J* 2012;58:15–18.
- [195] Tran HA, Pollema TL, Silva Enciso J, Greenberg BH, Barnard DD, Adler ED *et al.* Durable biventricular support using right atrial placement of the HeartWare HVAD. *ASAIO J* 2017;64:323–7.
- [196] Krabatsch T, Potapov E, Stepanenko A, Schweiger M, Kukucka M, Huebler M *et al.* Biventricular circulatory support with two miniaturized implantable assist devices. *Circulation* 2011;124:S179–86.
- [197] Torregrossa G, Morshuis M, Varghese R, Hosseinian L, Vida V, Tarzia V *et al.* Results with SynCardia total artificial heart beyond 1 year. *ASAIO J* 2014;60:626–34.
- [198] Thanavaro KL, Tang DG, Kasirajan V, Shah KB. Clinical indications for implantation of the total artificial heart. *ASAIO J* 2014;60:594–6.
- [199] Copeland JG, Copeland H, Gustafson M, Mineburg N, Covington D, Smith RG *et al.* Experience with more than 100 total artificial heart implants. *J Thorac Cardiovasc Surg* 2012;143:727–34.
- [200] Nguyen A, Pozzi M, Mastroianni C, Leger P, Loisanche D, Pavie A *et al.* Bridge to transplantation using paracorporeal biventricular assist devices or the syncardia temporary total artificial heart: is there a difference? *J Cardiovasc Surg (Torino)* 2015;56:493–502.
- [201] Kirsch ME, Nguyen A, Mastroianni C, Pozzi M, Leger P, Nicolescu M *et al.* SynCardia temporary total artificial heart as bridge to transplantation: current results at la pitie hospital. *Ann Thorac Surg* 2013;95: 1640–6.
- [202] Carpentier A, Latremouille C, Cholley B, Smadja DM, Roussel JC, Boissier E *et al.* First clinical use of a bioprosthetic total artificial heart: report of two cases. *Lancet* 2015;386:1556–63.
- [203] Kremer J, Farag M, Arif R, Brcic A, Sabashnikov A, Schmack B *et al.* Total artificial heart implantation after undifferentiated high-grade sarcoma excision. *Med Sci Monit Basic Res* 2016;22:128–31.
- [204] Reich H, Czer L, Bannykh S, De Robertis M, Wolin E, Amersi F *et al.* Total artificial heart bridge to transplantation for a patient with occult intracardiac malignancy: case report. *Transplant Proc* 2015;47: 2291–4.
- [205] Ried M, Rupperecht L, Hirt S, Zausig Y, Grube M, Resch M *et al.* Sequential therapy of primary cardiac lymphoma with cardiectomy, total artificial heart support, and cardiac transplantation. *J Heart Lung Transplant* 2010;29:707–9.
- [206] Strueber M, Schmitto JD, Kutschka I, Haverich A. Placement of 2 implantable centrifugal pumps to serve as a total artificial heart after cardiectomy. *J Thorac Cardiovasc Surg* 2012;143:507–9.
- [207] Knezevic I, Jelenc M, Danojevic N, Racic M, Poglajen G, Ksela J *et al.* Use of a totally artificial heart for a complex postinfarction ventricular septal defect. *Heart Surg Forum* 2013;16:155–7.
- [208] Ashfaq A, Jaroszewski DE, Pajaro OE, Arabia FA. The role of the total artificial heart in the treatment of post-myocardial infarction ventricular septal defect. *J Thorac Cardiovasc Surg* 2013;145:e25–6.
- [209] Morales DL, Khan MS, Gottlieb EA, Krishnamurthy R, Dreyer WJ, Adachi I. Implantation of total artificial heart in congenital heart disease. *Semin Thorac Cardiovasc Surg* 2012;24:142–3.
- [210] Rossano JW, Goldberg DJ, Fuller S, Ravishanker C, Montenegro LM, Gaynor JW. Successful use of the total artificial heart in the failing Fontan circulation. *Ann Thorac Surg* 2014;97:1438–40.
- [211] Copeland J, Copeland H, Nolan P, Gustafson M, Slepien M, Smith R. Results with an anticoagulation protocol in 99 SynCardia total artificial heart recipients. *ASAIO J* 2013;59:216–20.
- [212] Lavee J, Mulzer J, Krabatsch T, Marasco S, McGiffin D, Garbade J *et al.* An international multicenter experience of biventricular support with HeartMate 3 ventricular assist systems. *J Heart Lung Transplant* 2018;37:1399–402.
- [213] Eulert-Grehn JJ, Lanmuller P, Schonrath F, Solowjowa N, Muller M, Mulzer J *et al.* Two implantable continuous-flow ventricular assist devices in a biventricular configuration: technique and results. *Interact CardioVasc Thorac Surg* 2018;27:938–42.
- [214] Broussard D, Donaldson E, Falterman J, Bates M. Anesthesia for left ventricular assist device insertion: a case series and review. *Ochsner J* 2011; 11:70–7.
- [215] Kocabas S, Askar FZ, Yagdi T, Engin C, Ozbaran M. Anesthesia for ventricular assist device placement: experience from a single center. *Transplant Proc* 2013;45:1005–8.
- [216] Sanjay OP. Perioperative management of left ventricular assist devices. *Ann Card Anaesth* 2016;19:S19–20.
- [217] Hind D, Calvert N, McWilliams R, Davidson A, Paisley S, Beverley C *et al.* Ultrasonic locating devices for central venous cannulation: meta-analysis. *BMJ* 2003;327:361.
- [218] Long DA, Coulthard MG. Effect of heparin-bonded central venous catheters on the incidence of catheter-related thrombosis and infection in children and adults. *Anaesth Intensive Care* 2006;34:481.
- [219] Palepu GB, Deven J, Subrahmanyam M, Mohan S. Impact of ultrasonography on central venous catheter insertion in intensive care. *Indian J Radiol Imaging* 2009;19:191–8.
- [220] Calvert N, Hind D, McWilliams RG, Thomas SM, Beverley C, Davidson A. The effectiveness and cost-effectiveness of ultrasound locating devices for central venous access: a systematic review and economic evaluation. *Health Technol Assess* 2003;7:1–84.
- [221] Schwann NM, Hillel Z, Hoeft A, Barash P, Mohnle P, Miao Y *et al.* Lack of effectiveness of the pulmonary artery catheter in cardiac surgery. *Anesth Analg* 2011;113:994–1002.
- [222] Cowie BS. Does the pulmonary artery catheter still have a role in the perioperative period? *Anaesth Intensive Care* 2011;39:345–55.
- [223] Kanchi M. Do we need a pulmonary artery catheter in cardiac anaesthesia?—An Indian perspective. *Ann Card Anaesth* 2011;14:25–9.
- [224] El-Magharbel I. Ventricular assist devices and anesthesia. *Semin Cardiothorac Vasc Anesth* 2005;9:241–9.

- [225] Myles PS, Leslie K, McNeil J, Forbes A, Chan MT. Bispectral index monitoring to prevent awareness during anaesthesia: the B-Aware randomised controlled trial. *Lancet* 2004;363:1757–63.
- [226] Schon J, Heringlake M, Berger KU, Volker Groesdonk H, Sedemund-Adib B, Paarmann H. Relationship between mixed venous oxygen saturation and regional cerebral oxygenation in awake, spontaneously breathing cardiac surgery patients. *Minerva Anestesiologica* 2011;77:952–8.
- [227] Morel J, Salard M, Castelain C, Bayon MC, Lambert P, Vola M *et al.* Haemodynamic consequences of etomidate administration in elective cardiac surgery: a randomized double-blinded study. *Br J Anaesth* 2011;107:503–9.
- [228] Aviado DM Jr, Ling JS, Schmidt CF. Effects of anoxia on pulmonary circulation: reflex pulmonary vasoconstriction. *Am J Physiol* 1957;189:253–62.
- [229] Walkey AJ, Goligher E, Del Sorbo L, Hodgson C, Adhikari NK, Wunsch H *et al.* Low tidal volume versus non-volume-limited strategies for patients with acute respiratory distress syndrome: a systematic review and meta-analysis. *Ann Am Thorac Soc* 2017;14:S271–9.
- [230] Chummanvej S, Wood MJ, MacGillivray TE, Melo MF. Perioperative echocardiographic examination for ventricular assist device implantation. *Anesth Analg* 2007;105:583–601.
- [231] Scalia GM, McCarthy PM, Savage RM, Smedira NG, Thomas JD. Clinical utility of echocardiography in the management of implantable ventricular assist devices. *J Am Soc Echocardiogr* 2000;13:754–63.
- [232] Lang RM, Badano LP, Mor-Avi V, Afzalalo J, Armstrong A, Ernande L *et al.* Recommendations for cardiac chamber quantification by echocardiography in adults: an update from the American Society of Echocardiography and the European Association of Cardiovascular Imaging. *Eur Heart J Cardiovasc Imaging* 2015;16:233–70.
- [233] Nicoara A, Mackensen GB, Podgoreanu MV, Milano CA, Mathew JP, Swaminathan M. Malpositioned left ventricular assist device cannula: diagnosis and management with transesophageal echocardiography guidance. *Anesth Analg* 2007;105:1574–6.
- [234] Pieri M, Scandroglio AM, Kukucka M, Kretschmar A, Dreyse S, Falk V *et al.* Heart failure after 5 years on LVAD: diagnosis and treatment of outflow graft obstruction. *ASAIO J* 2017;63:e1–2.
- [235] Wagner F, Dandel M, Gunther G, Loebe M, Schulze-Neick I, Laucke U *et al.* Nitric oxide inhalation in the treatment of right ventricular dysfunction following left ventricular assist device implantation. *Circulation* 1997;96:II-291–6.
- [236] Argenziano M, Choudhri AF, Moazami N, Rose EA, Smith CR, Levin HR *et al.* Randomized, double-blind trial of inhaled nitric oxide in LVAD recipients with pulmonary hypertension. *Ann Thorac Surg* 1998;65:340–5.
- [237] Potapov E, Meyer D, Swaminathan M, Ramsay M, El Banayosy A, Diehl C *et al.* Inhaled nitric oxide after left ventricular assist device implantation: a prospective, randomized, double-blind, multicenter, placebo-controlled trial. *J Heart Lung Transplant* 2011;30:870–8.
- [238] Benedetto M, Romano R, Baca G, Sarridou D, Fischer A, Simon A *et al.* Inhaled nitric oxide in cardiac surgery: evidence or tradition? *Nitric Oxide* 2015;49:67–79.
- [239] Peura JL, Colvin-Adams M, Francis GS, Grady KL, Hoffman TM, Jessup M *et al.* Recommendations for the use of mechanical circulatory support: device strategies and patient selection: a scientific statement from the American Heart Association. *Circulation* 2012;126:2648–67.
- [240] Bolliger D, Tanaka KA. Roles of thrombelastography and thromboelastometry for patient blood management in cardiac surgery. *Transfus Med Rev* 2013;27:213–20.
- [241] Wikkelsøe AJ, Afshari A, Wetterslev J, Brok J, Moeller AM. Monitoring patients at risk of massive transfusion with thrombelastography or thromboelastometry: a systematic review. *Acta Anaesthesiol Scand* 2011;55:1174–89.
- [242] Deppe AC, Weber C, Zimmermann J, Kuhn EW, Slottoch I, Liakopoulos OJ *et al.* Point-of-care thromboelastography/thromboelastometry-based coagulation management in cardiac surgery: a meta-analysis of 8332 patients. *J Surg Res* 2016;203:424–33.
- [243] Heringlake M, Garbers C, Kabler JH, Anderson I, Heinze H, Schon J *et al.* Preoperative cerebral oxygen saturation and clinical outcomes in cardiac surgery. *Anesthesiology* 2011;114:58–69.
- [244] Haglund NA, Burdorf A, Jones T, Shostrom V, Um J, Ryan T *et al.* Inhaled milrinone after left ventricular assist device implantation. *J Card Fail* 2015;21:792–7.
- [245] Klodell CT Jr, Morey TE, Lobato EB, Aranda JM Jr, Staples ED, Schofield RS *et al.* Effect of sildenafil on pulmonary artery pressure, systemic pressure, and nitric oxide utilization in patients with left ventricular assist devices. *Ann Thorac Surg* 2007;83:68–71; discussion 71.
- [246] Trachte AL, Lobato EB, Urdaneta F, Hess PJ, Klodell CT, Martin TD *et al.* Oral sildenafil reduces pulmonary hypertension after cardiac surgery. *Ann Thorac Surg* 2005;79:194–7.
- [247] Netuka I, Sood P, Pya Y, Zimpfer D, Krabatsch T, Garbade J *et al.* Fully magnetically levitated left ventricular assist system for treating advanced HF: a multicenter study. *J Am Coll Cardiol* 2015;66:2579–89.
- [248] Cheng R, Ramzy D, Azarbal B, Arabia FA, Esmailian F, Czer LS *et al.* Device strategies for patients in INTERMACS profiles 1 and 2 cardiogenic shock: double bridge with extracorporeal membrane oxygenation and initial implant of more durable devices. *Artif Organs* 2017;41:224–32.
- [249] Frazier OH, Gregoric ID, Cohn WE. Initial experience with non-thoracic, extraperitoneal, off-pump insertion of the Jarvik 2000 Heart in patients with previous median sternotomy. *J Heart Lung Transplant* 2006;25:499–503.
- [250] Potapov EV, Kukucka M, Falk V, Krabatsch T. Off-pump implantation of the HeartMate 3 left ventricular assist device through a bilateral thoracotomy approach. *J Thorac Cardiovasc Surg* 2017;153:104–5.
- [251] Hanke JS, Krabatsch T, Rojas SV, Deniz E, Ismail I, Martens A *et al.* In vitro evaluation of inflow cannula fixation techniques in left ventricular assist device surgery. *Artif Organs* 2017;41:272–5.
- [252] Hanke JS, Rojas SV, Avsar M, Haverich A, Schmitto JD. Minimally-invasive LVAD Implantation: state of the Art. *Curr Cardiol Rev* 2015;11:246–51.
- [253] Muthiah K, Phan J, Robson D, Macdonald PS, Keogh AM, Kotlyar E *et al.* Centrifugal continuous-flow left ventricular assist device in patients with hypertrophic cardiomyopathy: a case series. *ASAIO J* 2013;59:183–7.
- [254] Deo SV, Park SJ. Centrifugal continuous-flow left ventricular assist device in patients with hypertrophic cardiomyopathy: a case series. *ASAIO J* 2013;59:97–8.
- [255] Hanke JS, Rojas SV, Cvitkovic T, Wiegmann B, Horke A, Warnecke G *et al.* First results of HeartWare left ventricular assist device implantation with tunnelling of the outflow graft through the transverse sinus. *Interact CardioVasc Thorac Surg* 2017;25:503–8.
- [256] Nawata K, Nishimura T, Kyo S, Hisagi M, Kinoshita O, Saito A *et al.* Outcomes of midterm circulatory support by left ventricular assist device implantation with descending aortic anastomosis. *J Artif Organs* 2010;13:197–201.
- [257] Zucchetta F, Tarzia V, Bottio T, Gerosa G. The Jarvik-2000 ventricular assist device implantation: how we do it. *Ann Cardiothorac Surg* 2014;3:525–31.
- [258] Hanke JS, Rojas SV, Martens A, Schmitto JD. Minimally invasive left ventricular assist device implantation with outflow graft anastomosis to the innominate artery. *J Thorac Cardiovasc Surg* 2015;149:e69–70.
- [259] Dean D, Kallel F, Ewald GA, Tatoes A, Sheridan BC, Brewer RJ *et al.* Reduction in driveline infection rates: results from the HeartMate II Multicenter Driveline Silicone Skin Interface (SSI) Registry. *J Heart Lung Transplant* 2015;34:781–9.
- [260] Schibilsky D, Benk C, Haller C, Berchtold-Herz M, Siepe M, Beyersdorf F *et al.* Double tunnel technique for the LVAD driveline: improved management regarding driveline infections. *J Artif Organs* 2012;15:44–8.
- [261] Svenarud P, Persson M, van der Linden J. Effect of CO<sub>2</sub> insufflation on the number and behavior of air microemboli in open-heart surgery: a randomized clinical trial. *Circulation* 2004;109:1127–32.
- [262] Martens S, Dietrich M, Wals S, Steffen S, Wimmer-Greinecker G, Moritz A. Conventional carbon dioxide application does not reduce cerebral or myocardial damage in open heart surgery. *Ann Thorac Surg* 2001;72:1940–4.
- [263] Schmitto JD, Rojas SV, Hanke JS, Avsar M, Haverich A. Minimally invasive left ventricular assist device implantation after cardiac recovery: surgical technical considerations. *Artif Organs* 2014;38:507–10.
- [264] Stulak JM, Romans T, Cowger J, Romano MA, Haft JW, Aaronson KD *et al.* Delayed sternal closure does not increase late infection risk in patients undergoing left ventricular assist device implantation. *J Heart Lung Transplant* 2012;31:1115–19.
- [265] Bhamra JK, Bansal U, Winger DG, Teuteberg JJ, Bermudez C, Kormos RL *et al.* Clinical experience with temporary right ventricular mechanical circulatory support. *J Thorac Cardiovasc Surg* 2018;156:1885–91.
- [266] Potapov EV, Kukucka M, Falk V, Krabatsch T. Biventricular support using 2 HeartMate 3 pumps. *J Heart Lung Transplant* 2016;35:1268–70.
- [267] Potapov EV, Stepanenko A, Hennig E, Hetzer R, Krabatsch T. A titanium plug simplifies left ventricular assist device removal after myocardial recovery. *J Heart Lung Transplant* 2010;29:1316–17.

- [268] Dykes JC, Reinhartz O, Almond CS, Yarlagadda V, Murray J, Rosenthal DN *et al.* Alternative strategy for biventricular assist device in an infant with hypertrophic cardiomyopathy. *Ann Thorac Surg* 2017;104:e185–e86.
- [269] Loebe M, Bruckner B, Reardon MJ, van Doorn E, Estep J, Gregoric I *et al.* Initial clinical experience of total cardiac replacement with dual HeartMate-II axial flow pumps for severe biventricular heart failure. *Methodist Debaque Cardiovasc J* 2011;7:40–4.
- [270] Pirk J, Maly J, Szarszoi O, Urban M, Kotulak T, Riha H *et al.* Total artificial heart support with two continuous-flow ventricular assist devices in a patient with an infiltrating cardiac sarcoma. *ASAIO J* 2013;59:178–80.
- [271] Haj-Yahia S, Birks EJ, Dreyfus G, Khaghani A. Limited surgical approach for explanting the HeartMate II left ventricular assist device after myocardial recovery. *J Thorac Cardiovasc Surg* 2008;135:453–4.
- [272] Cohn WE, Gregoric ID, Radovancevic B, Frazier OH. A felt plug simplifies left ventricular assist device removal after successful bridge to recovery. *J Heart Lung Transplant* 2007;26:1209–11.
- [273] Pettit SJ, Shapiro LM, Lewis C, Parameshwar JK, Tsui SS. Percutaneous withdrawal of HeartWare HVAD left ventricular assist device support. *J Heart Lung Transplant* 2015;34:990–2.
- [274] Choi JH, Weber MP, Horan DP, Luc JGY, Phan K, Patel S *et al.* Left ventricular assist device decommissioning compared with explantation for ventricular recovery: a systematic review. *ASAIO J* 2018;1–6.
- [275] VanderPluym CJ, Cedars A, Eghtesady P, Maxwell BG, Gelow JM, Burchill LJ *et al.* Outcomes following implantation of mechanical circulatory support in adults with congenital heart disease: an analysis of the Interagency Registry for Mechanically Assisted Circulatory Support (INTERMACS). *J Heart Lung Transplant* 2017;37:89–99.
- [276] de By TMMH, Schweiger M, Waheed H, Berger F, Hübler M, Özbaran M *et al.* The European Registry for Patients with Mechanical Circulatory Support (EUROMACS): first EUROMACS Paediatric (Paedi-EUROMACS) report. *Eur J Cardiothorac Surg* 2018;54:800–8.
- [277] Schweiger M, Miera O, de By TMMH, Hubler M, Berger F, Ozbaran M *et al.* Cerebral strokes in children on intracorporeal ventricular assist devices: analysis of the EUROMACS Registry. *Eur J Cardiothorac Surg* 2017;53:416–21.
- [278] Villa CR, Khan MS, Zafar F, Morales DLS, Lorts A. United States trends in pediatric ventricular assist implantation as bridge to transplantation. *ASAIO J* 2017;63:470–5.
- [279] Rossano JW, Lorts A, VanderPluym CJ, Jeewa A, Guleserian KJ, Bleiweis MS *et al.* Outcomes of pediatric patients supported with continuous-flow ventricular assist devices: a report from the Pediatric Interagency Registry for Mechanical Circulatory Support (PediMACS). *J Heart Lung Transplant* 2016;35:585–90.
- [280] Miera O, Potapov EV, Redlin M, Stepanenko A, Berger F, Hetzer R *et al.* First experiences with the HeartWare ventricular assist system in children. *Ann Thorac Surg* 2011;91:1256–60.
- [281] Miera O, Kirk R, Buchholz H, Schmitt KR, VanderPluym C, Rebeyka IM *et al.* A multicenter study of the HeartWare ventricular assist device in small children. *J Heart Lung Transplant* 2016;35:679–81.
- [282] Chen S, Lin A, Liu E, Gowan M, May LJ, Doan LN *et al.* Outpatient outcomes of pediatric patients with left ventricular assist devices. *ASAIO J* 2016;62:163–8.
- [283] Adachi I, Williams E, Jeewa A, Elias B, McKenzie ED. Mechanically assisted Fontan completion: a new approach for the failing Glenn circulation due to isolated ventricular dysfunction. *J Heart Lung Transplant* 2016;35:1380–1.
- [284] Schweiger M, Vanderpluym C, Jeewa A, Canter CE, Jansz P, Parrino PE *et al.* Outpatient management of intra-corporeal left ventricular assist device system in children: a multi-center experience. *Am J Transplant* 2015;15:453–60.
- [285] Conway J, MieraOHendersonHT, Vanderplym C, Buchholz H, Fenton M *et al.* Global experience with the HeartWare HVAD® in pediatric patients: a preliminary analysis. *J Heart Lung Transplant* 2016;35:1.
- [286] Lowry AW, Adachi I, Gregoric ID, Jeewa A, Morales DL. The potential to avoid heart transplantation in children: outpatient bridge to recovery with an intracorporeal continuous-flow left ventricular assist device in a 14-year-old. *Congenit Heart Dis* 2012;7:E91.
- [287] Conway J, St Louis J, Morales DL, Law S, Tjossem C, Humpl T. Delineating survival outcomes in children <10 kg bridged to transplant or recovery with the Berlin Heart EXCOR ventricular assist device. *JACC Heart Fail* 2015;3:70–7.
- [288] Morales DL, Zafar F, Almond CS, Canter C, Fynn-Thompson F, Conway J *et al.* Berlin Heart EXCOR use in patients with congenital heart disease. *J Heart Lung Transplant* 2017;36:1209–16.
- [289] Cabrera AG, Sundareswaran KS, Samayoa AX, Jeewa A, McKenzie ED, Rossano JW *et al.* Outcomes of pediatric patients supported by the HeartMate II left ventricular assist device in the United States. *J Heart Lung Transplant* 2013;32:1107–13.
- [290] Blume ED, Rosenthal DN, Rossano JW, Baldwin JT, Eghtesady P, Morales DL *et al.* Outcomes of children implanted with ventricular assist devices in the United States: first analysis of the Pediatric Interagency Registry for Mechanical Circulatory Support (PediMACS). *J Heart Lung Transplant* 2016;35:578–84.
- [291] Poh CL, Chilette R, Zannino D, Brizard C, Konstantinov IE, Horton S *et al.* Ventricular assist device support in patients with single ventricles: the Melbourne experience. *Interact CardioVasc Thorac Surg* 2017;25:310–16.
- [292] Weinstein S, Bello R, Pizarro C, Fynn-Thompson F, Kirklín J, Guleserian K *et al.* The use of the Berlin heart EXCOR in patients with functional single ventricle. *J Thorac Cardiovasc Surg* 2014;147:697–705.
- [293] Irving CA, Cassidy JV, Kirk RC, Griselli M, Hasan A, Crossland DS. Successful bridge to transplant with the Berlin heart after cavopulmonary shunt. *J Heart Lung Transplant* 2009;28:399–401.
- [294] Throckmorton AL, Lopez-Isaza S, Downs EA, Chopski SG, Gangemi JJ, Moskowitz W. A viable therapeutic option: mechanical circulatory support of the failing Fontan physiology. *Pediatr Cardiol* 2013;34:1357–65.
- [295] Giridharan GA, Koenig SC, Kennington J, Sobieski MA, Chen J, Frankel SH *et al.* Performance evaluation of a pediatric viscous impeller pump for Fontan cavopulmonary assist. *J Thorac Cardiovasc Surg* 2013;145:249–57.
- [296] Haggerty CM, Fynn-Thompson F, McElhinney DB, Valente AM, Saikrishnan N, Del Nido PJ *et al.* Experimental and numeric investigation of Impella pumps as cavopulmonary assistance for a failing Fontan. *J Thorac Cardiovasc Surg* 2012;144:563–9.
- [297] Pretre R, Haussler A, Bettex D, Genoni M. Right-sided univentricular cardiac assistance in a failing Fontan circulation. *Ann Thorac Surg* 2008;86:1018–20.
- [298] Rodefeld MD, Coats B, Fisher T, Giridharan GA, Chen J, Brown JW *et al.* Cavopulmonary assist for the univentricular Fontan circulation: von Karman viscous impeller pump. *J Thorac Cardiovasc Surg* 2010;140:529–36.
- [299] Pace Napoleone C, Cascarano MT, Deorsola L, Valori A. Ventricular assist device in a failing total cavopulmonary connection: a new step-by-step approach. *Interact CardioVasc Thorac Surg* 2017;26:341–2.
- [300] Wells D, Villa CR, Simon Morales DL. The 50/50 cc total artificial heart trial: extending the benefits of the total artificial heart to underserved populations. *Semin Thorac Cardiovasc Surg Pediatr Card Surg Annu* 2017;20:16–19.
- [301] Morales DLS, Lorts A, Rizwan R, Zafar F, Arabia FA, Villa CR. Worldwide experience with the SynCardia total artificial heart in the pediatric population. *ASAIO J* 2017;63:518–19.
- [302] Steiner JM, Krieger EV, Stout KK, Stempien-Otero A, Mahr C, Mokadam NA *et al.* Durable mechanical circulatory support in teenagers and adults with congenital heart disease: a systematic review. *Int J Cardiol* 2017;245:135–40.
- [303] Stokes MB, Saxena P, McGiffin DC, Marasco S, Leet AS, Bergin P. Successful bridge to orthotopic cardiac transplantation with implantation of a HeartWare HVAD in management of systemic right ventricular failure in a patient with transposition of the great arteries and previous atrial switch procedure. *Heart Lung Circ* 2016;25:e69–71.
- [304] Tanoue Y, Jinzai Y, Tominaga R. Jarvik 2000 axial-flow ventricular assist device placement to a systemic morphologic right ventricle in congenitally corrected transposition of the great arteries. *J Artif Organs* 2016;19:97–9.
- [305] Maly J, Netuka I, Besik J, Dorazilova Z, Pirk J, Szarszoi O. Bridge to transplantation with long-term mechanical assist device in adults after the Mustard procedure. *J Heart Lung Transplant* 2015;34:1177–81.
- [306] Dakkak AR, Sindermann JR, Dell'Aquila AM, Welp HA, Martens S, Scherer M. Implanting a nonpulsatile axial flow left ventricular assist device as a bridge to transplant for systemic ventricular failure after a mustard procedure. *Exp Clin Transplant* 2015;13:485–7.
- [307] Schweiger M, Falk V, Biry M, Hubler M, Wilhelm MJ. Biventricular failure in dextro-transposition of the great arteries corrected with the Mustard procedure: VAD support of the systemic ventricle is enough. *Int J Artif Organs* 2015;38:233–5.
- [308] Fraser CD Jr, Jaquiss RD, Rosenthal DN, Humpl T, Canter CE, Blackstone EH *et al.* Prospective trial of a pediatric ventricular assist device. *N Engl J Med* 2012;367:532–41.

- [309] Morales DL, Almond CS, Jaquiss RD, Rosenthal DN, Naftel DC, Massicotte MP *et al.* Bridging children of all sizes to cardiac transplantation: the initial multicenter North American experience with the Berlin Heart EXCOR ventricular assist device. *J Heart Lung Transplant* 2011;30:1–8.
- [310] Almond CS, Morales DL, Blackstone EH, Turrentine MW, Imamura M, Massicotte MP *et al.* Berlin Heart EXCOR pediatric ventricular assist device for bridge to heart transplantation in US children. *Circulation* 2013;127:1702–11.
- [311] Zafar F, Villa CR, Morales DL, Blume ED, Rosenthal DN, Kirklín JK *et al.* Does small size matter with continuous flow devices? Analysis of the INTERMACS database of adults with BSA  $\leq$ 1.5 m<sup>2</sup>. *JACC Heart Fail* 2017;5:123–31.
- [312] Ferng AS, Oliva I, Jokerst C, Avery R, Connell AM, Tran PL *et al.* Translating of first North American 50 and 70 cc total artificial heart virtual and clinical implantations: utility of 3D computed tomography to test fit devices. *Artif Organs* 2017;41:727–34.
- [313] Moore RA, Lorts A, Madueme PC, Taylor MD, Morales DL. Virtual implantation of the 50cc SynCardia total artificial heart. *J Heart Lung Transplant* 2016;35:824–7.
- [314] Moore RA, Madueme PC, Lorts A, Morales DL, Taylor MD. Virtual implantation evaluation of the total artificial heart and compatibility: beyond standard fit criteria. *J Heart Lung Transplant* 2014;33:1180–3.
- [315] Maxwell BG, Wong JK, Sheikh AY, Lee PHU, Lobato RL. Heart transplantation with or without prior mechanical circulatory support in adults with congenital heart disease. *Eur J Cardiothorac Surg* 2014;45:842–6.
- [316] Gelow JM, Song HK, Weiss JB, Mudd JO, Broberg CS. Organ allocation in adults with congenital heart disease listed for heart transplant: impact of ventricular assist devices. *J Heart Lung Transplant* 2013;32:1059–64.
- [317] Maltais S, Costello WT, Billings FT 4th, Bick JS, Byrne JG, Ahmad RM *et al.* Episodic monoplane transesophageal echocardiography impacts postoperative management of the cardiac surgery patient. *J Cardiothorac Vasc Anesth* 2013;27:665–9.
- [318] Ranucci M. Which cardiac surgical patients can benefit from placement of a pulmonary artery catheter? *Crit Care* 2006;10:S6.
- [319] Geisen M, Spray D, Nicholas Fletcher S. Echocardiography-based hemodynamic management in the cardiac surgical intensive care unit. *J Cardiothorac Vasc Anesth* 2014;28:733–44.
- [320] Kato TS, Jiang J, Schulze PC, Jorde U, Uriel N, Kitada S *et al.* Serial echocardiography using tissue Doppler and speckle tracking imaging to monitor right ventricular failure before and after left ventricular assist device surgery. *JACC Heart Fail* 2013;1:216–22.
- [321] Riebandt J, Haberl T, Wiedemann D, Moayedifar R, Schloegelhofer T, Mahr S *et al.* Extracorporeal membrane oxygenation support for right ventricular failure after left ventricular assist device implantation; temporary right ventricular support following left ventricle assist device implantation: a comparison of two techniques. *Eur J Cardiothorac Surg* 2017;19:49–55.
- [322] Takeda K, Li B, Garan AR, Topkara VK, Han J, Colombo PC *et al.* Improved outcomes from extracorporeal membrane oxygenation versus ventricular assist device temporary support of primary graft dysfunction in heart transplant. *J Heart Lung Transplant* 2017;36:650–6.
- [323] Antoniou T, Prokakis C, Athanasopoulos G, Thanopoulos A, Rellia P, Zarkalis D *et al.* Inhaled nitric oxide plus iloprost in the setting of post-left assist device right heart dysfunction. *Ann Thorac Surg* 2012;94:792–8.
- [324] Groves DS, Blum FE, Huffmyer JL, Kennedy JL, Ahmad HB, Durieux ME *et al.* Effects of early inhaled epoprostenol therapy on pulmonary artery pressure and blood loss during LVAD placement. *J Cardiothorac Vasc Anesth* 2014;28:652–60.
- [325] Hamdan R, Mansour H, Nassar P, Saab M. Prevention of right heart failure after left ventricular assist device implantation by phosphodiesterase 5 inhibitor. *Artif Organs* 2014;38:963–7.
- [326] Lovich MA, Pezone MJ, Wakim MG, Denton RJ, Maslov MY, Murray MR *et al.* Inhaled nitric oxide augments left ventricular assist device capacity by ameliorating secondary right ventricular failure. *ASAIO J* 2015;61:379–85.
- [327] Sabato LA, Salerno DM, Moretz JD, Jennings DL, Critoph C, Green G *et al.* Inhaled pulmonary vasodilator therapy for management of right ventricular dysfunction after left ventricular assist device placement and cardiac transplantation. Clinical outcomes of patients treated with pulmonary vasodilators early and in high dose after left ventricular assist device implantation. *Pharmacotherapy* 2017;37:944–55.
- [328] De Backer D, Biston P, Devriendt J, Madl C, Chochrad D, Aldecoa C *et al.* Comparison of dopamine and norepinephrine in the treatment of shock. *N Engl J Med* 2010;362:779–89.
- [329] Havel C, Arrich J, Losert H, Gamper G, Mullner M, Herkner H *et al.* Vasopressors for hypotensive shock. *Cochrane Database Syst Rev* 2011;5. Art. No.: CD003709. doi: 10.1002/14651858.CD003709.pub3.
- [330] Levy B, Perez P, Perny J, Thivillier C, Gerard A. Comparison of norepinephrine-dobutamine to epinephrine for hemodynamics, lactate metabolism, and organ function variables in cardiogenic shock. A prospective, randomized pilot study. *Crit Care Med* 2011;39:450–5.
- [331] Tarvasmaki T, Lassus J, Varpula M, Sionis A, Sund R, Kober L *et al.* Current real-life use of vasopressors and inotropes in cardiogenic shock - adrenaline use is associated with excess organ injury and mortality. *Crit Care (London, England)* 2016;20:208.
- [332] Burkhardt BE, Rucker G, Stiller B. Prophylactic milrinone for the prevention of low cardiac output syndrome and mortality in children undergoing surgery for congenital heart disease. *Cochrane Database Syst Rev* 2015; 3. Art. No.: CD009515. doi: 10.1002/14651858.CD009515.pub2.
- [333] You Z, Huang L, Cheng X, Wu Q, Jiang X, Wu Y. Effect of milrinone on cardiac functions in patients undergoing coronary artery bypass graft: a meta-analysis of randomized clinical trials. *Drug Des Devel Ther* 2016; 10:53–8.
- [334] Landoni G, Lomivorotov VV, Alvaro G, Lobreglio R, Pisano A, Guarracino F *et al.* Levosimendan for hemodynamic support after cardiac surgery. *N Engl J Med* 2017;376:2021–31.
- [335] Mehta RH, Leimberger JD, van Diepen S, Meza J, Wang A, Jankowich R *et al.* Levosimendan in patients with left ventricular dysfunction undergoing cardiac surgery. *N Engl J Med* 2017;376:2032–42.
- [336] Repesse X, Au SM, Brechot N, Trouillet JL, Leprince P, Chastre J *et al.* Recombinant factor VIIa for uncontrollable bleeding in patients with extracorporeal membrane oxygenation: report on 15 cases and literature review. *Crit Care* 2013;17:R55.
- [337] Gandhi MJ, Pierce RA, Zhang L, Moon MR, Despotis GJ, Moazami N. Use of activated recombinant factor VII for severe coagulopathy post ventricular assist device or orthotopic heart transplant. *J Cardiothorac Surg* 2007;2:32.
- [338] Slaughter MS, Naka Y, John R, Boyle A, Conte JV, Russell SD *et al.* Post-operative heparin may not be required for transitioning patients with a HeartMate II left ventricular assist system to long-term warfarin therapy. *J Heart Lung Transplant* 2010;29:616–24.
- [339] Joshi A, Smith D, Arora M, Poston R. Anticoagulant monitoring in ventricular assist device patients: a feasibility study. *Interact CardioVasc Thorac Surg* 2008;7:1035–8.
- [340] Bishop MA, Streiff MB, Ensor CR, Tedford RJ, Russell SD, Ross PA. Pharmacist-managed international normalized ratio patient self-testing is associated with increased time in therapeutic range in patients with left ventricular assist devices at an academic medical center. *ASAIO J* 2014;60:193–8.
- [341] Sandner SE, Riebandt J, Haberl T, Mahr S, Rajek A, Schima H *et al.* Low-molecular-weight heparin for anti-coagulation after left ventricular assist device implantation. *J Heart Lung Transplant* 2014;33:88–93.
- [342] Andreas M, Moayedifar R, Wieselthaler G, Wolzt M, Riebandt J, Haberl T *et al.* Increased thromboembolic events with dabigatran compared with vitamin K antagonism in left ventricular assist device patients: a randomized controlled pilot trial. *Circ Heart Fail* 2017;10:1–6.
- [343] Pereira NL, Chen D, Kushwaha SS, Park SJ. Discontinuation of antithrombotic therapy for a year or more in patients with continuous-flow left ventricular assist devices. *Interact CardioVasc Thorac Surg* 2010;11:503–5.
- [344] Axelrad JE, Pinsino A, Trinh PN, Thanataveerat A, Brooks C, Demmer RT *et al.* Limited usefulness of endoscopic evaluation in patients with continuous-flow left ventricular assist devices and gastrointestinal bleeding. *J Heart Lung Transplant* 2018;37:723–32.
- [345] Ben Gal T, Piepoli MF, Corra U, Conraads V, Adamopoulos S, Agostoni P *et al.* Exercise programs for LVAD supported patients: a snapshot from the ESC affiliated countries. *Int J Cardiol* 2015;201:215–19.
- [346] Piepoli MF, Conraads V, Corra U, Dickstein K, Francis DP, Jaarsma T *et al.* Exercise training in heart failure: from theory to practice. A consensus document of the Heart Failure Association and the European Association for Cardiovascular Prevention and Rehabilitation. *Eur J Heart Fail* 2011;13:347–57.
- [347] Hayes K, Leet AS, Bradley SJ, Holland AE. Effects of exercise training on exercise capacity and quality of life in patients with a left ventricular assist device: a preliminary randomized controlled trial. *J Heart Lung Transplant* 2012;31:729–34.
- [348] Marko C, Danzinger G, Kaferback M, Lackner T, Muller R, Zimpfer D *et al.* Safety and efficacy of cardiac rehabilitation for patients with

- continuous flow left ventricular assist devices. *Eur J Prev Cardiol* 2015; 22:1378–84.
- [349] Borg GA. Psychophysical bases of perceived exertion. *Med Sci Sports Exerc* 1982;14:377–81.
- [350] Carvalho VO, Mezzani A. Aerobic exercise training intensity in patients with chronic heart failure: principles of assessment and prescription. *Eur J Cardiovasc Prev Rehabil* 2011;18:5–14.
- [351] Marko C, Xhelili E, Lackner T, Zimpfer D, Schima H, Moscato F. Exercise performance during the first two years after left ventricular assist device implantation. *ASAIO J* 2017;63:408–13.
- [352] Vanhees L, Rauch B, Piepoli M, van Buuren F, Takken T, Borjesson M *et al.* Importance of characteristics and modalities of physical activity and exercise in the management of cardiovascular health in individuals with cardiovascular disease (part III). *Eur J Prev Cardiol* 2012;19: 1333–56.
- [353] Alsara O, Perez-Terzic C, Squires RW, Dandamudi S, Miranda WR, Park SJ *et al.* Is exercise training safe and beneficial in patients receiving left ventricular assist device therapy? *J Cardiopulm Rehabil Prev* 2014;34: 233–40.
- [354] Pamboukian SV, Tallaj JA, Brown RN, Holman WL, Blood M, George JF *et al.* Improvement in 2-year survival for ventricular assist device patients after implementation of an intensive surveillance protocol. *J Heart Lung Transplant* 2011;30:879–87.
- [355] Bieffer HR, Sundermann SH, Emmert MY, Hasenclever P, Lachat ML, Falk V *et al.* Experience with a “hotline” service for outpatients on a ventricular assist device. *Thorac Cardiovasc Surg* 2014;62:409–13.
- [356] Vierecke J, Schweiger M, Feldman D, Potapov E, Kaufmann F, Germinario L *et al.* Emergency procedures for patients with a continuous flow left ventricular assist device. *Emerg Med J* 2017;34:831–41.
- [357] Haglund NA, Davis ME, Tricarico NM, Keebler ME, Maltais S. Readmissions after continuous flow left ventricular assist device implantation: differences observed between two contemporary device types. *ASAIO J* 2015;61:410–16.
- [358] Chorpenning K, Brown MC, Voskoboinikov N, Reyes C, Dierlam AE, Tamez D. HeartWare controller logs a diagnostic tool and clinical management aid for the HVAD pump. *ASAIO J* 2014;60:115–18.
- [359] Lampert BC, Emani S. Remote hemodynamic monitoring for ambulatory left ventricular assist device patients. *J Thorac Dis* 2015;7:2165–71.
- [360] Pektok E, Demirozu ZT, Arat N, Yildiz O, Oklu E, Eker D *et al.* Remote monitoring of left ventricular assist device parameters after HeartAssist-5 implantation. *Artif Organs* 2013;37:820–5.
- [361] Noon GP, Loebe M. Current status of the MicroMed DeBakey noon ventricular assist device. *Tex Heart Inst J* 2010;37:652–3.
- [362] Schmitto JD, Hanke JS, Dogan G, Tessmann R, Jeevanandem V, Cohn WE *et al.* First implantation of a novel left ventricular assist device: the ReliantHeart aVAD. *Ann Thorac Surg* 2017;104:e311–13.
- [363] Hannan MM, Husain S, Mattner F, Danziger-Isakov L, Drew RJ, Corey GR *et al.* Working formulation for the standardization of definitions of infections in patients using ventricular assist devices. *J Heart Lung Transplant* 2011;30:375–84.
- [364] Goldstein DJ, Naftel D, Holman W, Bellumkonda L, Pamboukian SV, Pagani FD *et al.* Continuous-flow devices and percutaneous site infections: clinical outcomes. *J Heart Lung Transplant* 2012;31:1151–7.
- [365] John R, Aaronson KD, Pae WE, Acker MA, Hathaway DR, Najarian KB *et al.* Drive-line infections and sepsis in patients receiving the HVAD system as a left ventricular assist device. *J Heart Lung Transplant* 2014;33: 1066–73.
- [366] Angud M. Left ventricular assist device driveline infections: the Achilles’ heel of destination therapy. *AACN Adv Crit Care* 2015;26:300–5.
- [367] Wus L, Manning M, Entwistle JW 3rd. Left ventricular assist device driveline infection and the frequency of dressing change in hospitalized patients. *Heart Lung* 2015;44:225–9.
- [368] Hieda M, Sata M, Seguchi O, Yanase M, Murata Y, Sato T *et al.* Importance of early appropriate intervention including antibiotics and wound care for device-related infection in patients with left ventricular assist device. *Transplant Proc* 2014;46:907–10.
- [369] Nienaber JJ, Kusne S, Riaz T, Walker RC, Baddour LM, Wright AJ *et al.* Clinical manifestations and management of left ventricular assist device-associated infections. *Clin Infect Dis* 2013;57:1438–48.
- [370] Sperry BW, Fatemi O, Ruiz ME, Najjar SS. Late manifestation of a driveline infection after heart transplantation. *J Heart Lung Transplant* 2014; 33:324–5.
- [371] Walter V, Stock UA, Soriano-Romero M, Schnitzbauer A, Moritz A, Beiras-Fernandez A. Eradication of a chronic wound and driveline infection after redo-LVAD implantation. *J Cardiothorac Surg* 2014;9:63.
- [372] Maniar S, Kondareddy S, Topkara VK. Left ventricular assist device-related infections: past, present and future. *Expert Rev Med Devices* 2011;8:627–34.
- [373] Cagliostro B, Levin AP, Fried J, Stewart S, Parkis G, Mody KP *et al.* Continuous-flow left ventricular assist devices and usefulness of a standardized strategy to reduce drive-line infections. *J Heart Lung Transplant* 2016;35:108–14.
- [374] Trachtenberg BH, Cordero-Reyes A, Elias B, Loebe M. A review of infections in patients with left ventricular assist devices: prevention, diagnosis and management. *Methodist Debakey Cardiovasc J* 2015;11:28–32.
- [375] Yarboro LT, Bergin JD, Kennedy JL, Ballew CC, Benton EM, Ailawadi G *et al.* Technique for minimizing and treating driveline infections. *Ann Cardiothorac Surg* 2014;3:557–62.
- [376] Leuck AM. Left ventricular assist device driveline infections: recent advances and future goals. *J Thorac Dis* 2015;7:2151–7.
- [377] Lampert BC, Eckert C, Weaver S, Scanlon A, Lockard K, Allen C *et al.* Blood pressure control in continuous flow left ventricular assist devices: efficacy and impact on adverse events. *Ann Thorac Surg* 2014;97: 139–46.
- [378] Castagna F, McDonnell BJ, Stohr EJ, Yuzefpolskaya M, Trinh PN, Topkara VK *et al.* Non-invasive measurement of peripheral, central and 24-hour blood pressure in patients with continuous-flow left ventricular assist device. *J Heart Lung Transplant* 2017;36:694–7.
- [379] Bennett MK, Adaty S. Blood pressure management in mechanical circulatory support. *J Thorac Dis* 2015;7:2125–8.
- [380] Saeed O, Jermyn R, Kargoli F, Madan S, Mannem S, Gunda S *et al.* Blood pressure and adverse events during continuous flow left ventricular assist device support. *Circ Heart Fail* 2015;8:551–6.
- [381] Lanier GM, Orlanes K, Hayashi Y, Murphy J, Flannery M, Te-Frey R *et al.* Validity and reliability of a novel slow cuff-deflation system for noninvasive blood pressure monitoring in patients with continuous-flow left ventricular assist device. *Circ Heart Fail* 2013;6:1005–12.
- [382] Bennett MK, Roberts CA, Dordunoo D, Shah A, Russell SD. Ideal methodology to assess systemic blood pressure in patients with continuous-flow left ventricular assist devices. *J Heart Lung Transplant* 2010;29:593–4.
- [383] Wasson LT, Yuzefpolskaya M, Wakabayashi M, Takayama H, Naka Y, Uriel N *et al.* Hypertension: an unstudied potential risk factor for adverse outcomes during continuous flow ventricular assist device support. *Heart Fail Rev* 2015;20:317–22.
- [384] Patil NP, Mohite PN, Sabashnikov A, Dhar D, Weymann A, Zeriuoh M *et al.* Does postoperative blood pressure influence development of aortic regurgitation following continuous-flow left ventricular assist device implantation?. *Eur J Cardiothorac Surg* 2016;49:788–94.
- [385] Milano CA, Rogers JG, Tatooles AJ, Bhat G, Slaughter MS, Birks EJ *et al.* HVAD: the ENDURANCE supplemental trial. *JACC: Heart Failure* 2018;6: 792–802.
- [386] Canadian Medical Association. CMA Driver’s Guide: Determining Medical Fitness to Operate Motor Vehicles, 8th edn. Canadian Medical Association, Canada, 2012.
- [387] Simpson C, Dorian P, Gupta A, Hamilton R, Hart S, Hoffmaster B *et al.* Assessment of the cardiac patient for fitness to drive: drive subgroup executive summary. *Can J Cardiol* 2004;20:1314–20.
- [388] Emani S, O’Keefe CM, Wissman S, MacBair KS, White L, Hasan AK *et al.* 190 Driver’s education: a single center experience on the incidence and safety of driving with LVADs. *J Heart Lung Transplant* 2011; 30:570.
- [389] McKelvie RS, Moe GW, Cheung A, Costigan J, Ducharme A, Estrella-Holder E *et al.* The 2011 Canadian Cardiovascular Society heart failure management guidelines update: focus on sleep apnea, renal dysfunction, mechanical circulatory support, and palliative care. *Can J Cardiol* 2011;27:319–38.
- [390] Ambardekar AV, Cannon AP, Cleveland JC Jr, Brieke A, Lindenfeld J. Driving with a driveline: a survey of current practice patterns for allowing a patient supported with a left ventricular assist device to drive. *J Heart Lung Transplant* 2011;30:1204–5.
- [391] Baskett R, Crowell R, Freed D, Giannetti N, Simpson CS; Canadian Cardiovascular Society. Canadian Cardiovascular Society focused position statement update on assessment of the cardiac patient for fitness to drive: fitness following left ventricular assist device implantation. *Can J Cardiol* 2012;28:137–40.
- [392] Hanke JS, Riebandt J, Wahabzada M, Nur F, Wahabzada A, Dogan G *et al.* Driving after left ventricular assist device implantation. *Artif Organs* 2018;42:695–9.
- [393] Dandel M, Weng Y, Siniawski H, Stepanenko A, Krabatsch T, Potapov E *et al.* Heart failure reversal by ventricular unloading in patients with

- chronic cardiomyopathy: criteria for weaning from ventricular assist devices. *Eur Heart J* 2011;32:1148–60.
- [394] Segan LA, Nanayakkara SS, Leet AS, Vizi D, Kaye DM. Exercise hemodynamics as a predictor of myocardial recovery in LVAD patients. *ASAIO J* 2017;63:342–5.
- [395] Pan S, Aksut B, Wever-Pinzon OE, Rao SD, Levin AP, Garan AR *et al.* Incidence and predictors of myocardial recovery on long-term left ventricular assist device support: results from the United Network for organ sharing database. *J Heart Lung Transplant* 2015;34:1624–9.
- [396] Chaggar PS, Williams SG, Yonan N, Fildes J, Venkateswaran R, Shaw SM. Myocardial recovery with mechanical circulatory support. *Eur J Heart Fail* 2016;18:1220–7.
- [397] Drakos SG, Pagani FD, Lundberg MS, Baldwin TJ. Advancing the science of myocardial recovery with mechanical circulatory support: A Working Group of the National, Heart, Lung, and Blood Institute. *J Thorac Cardiovasc Surg* 2017;154:165–70.
- [398] Birks EJ, George RS, Hedger M, Bahrami T, Wilton P, Bowles CT *et al.* Reversal of severe heart failure with a continuous-flow left ventricular assist device and pharmacological therapy: a prospective study. *Circulation* 2011;123:381–90.
- [399] Jakovljevic DG, Yacoub MH, Schueler S, MacGowan GA, Velicki L, Seferovic PM *et al.* Left ventricular assist device as a bridge to recovery for patients with advanced heart failure. *J Am Coll Cardiol* 2017;69:1924–33.
- [400] Cavigelli-Brunner A, Schweiger M, Knirsch W, Stiasny B, Klingel K, Kretschmar O. VAD as bridge to recovery in anthracycline-induced cardiomyopathy and HHV6 myocarditis. *Pediatrics* 2014;134:E894–99.
- [401] Topkara VK, Garan AR, Fine B, Godier-Furnemont AF, Breskin A, Cagliostro B *et al.* Myocardial recovery in patients receiving contemporary left ventricular assist devices: results from the Interagency Registry for Mechanically Assisted Circulatory Support (INTERMACS). *Circ Heart Fail* 2016;9:1–11.
- [402] Lenneman AJ, Birks EJ. Treatment strategies for myocardial recovery in heart failure. *Current Treatment Options in Cardiovascular Medicine* 2014;16:287.
- [403] Ankersmit HJ, Ullrich R, Moser B, Hoetzenecker K, Hacker S, German P *et al.* Recovery from giant cell myocarditis with ECMO support and utilisation of polyclonal antithymocyte globulin: a case report. *Thorac Cardiovasc Surg* 2006;54:278–80.
- [404] Wiedemann D, Schloglhofer T, Riebandt J, Neuner M, Tschernko E, Schima H *et al.* Myocardial recovery in peripartum cardiomyopathy after hyperprolactinemia treatment on BIVAD. *ASAIO J* 2017;63:109–11.
- [405] Birks EJ, Drakos SG, Lowes BD, Patel SR, Selzman C, Slaughter MS *et al.* Outcome and primary endpoint results from a prospective multi-center study of myocardial recovery using LVADs: remission from Stage D Heart Failure (REStAGE-HF). *J Heart Lung Transplant* 2018;37:S142.
- [406] Potapov EV, Schweiger M, Krabatsch T. Percutaneous balloon occlusion of a left ventricular assist device outflow cannula to facilitate evaluation of myocardial recovery. *J Heart Lung Transplant* 2011;30:1300–1.
- [407] Knierim J, Heck R, Pieri M, Schoenrath F, Soltani S, Stawowy P *et al.* Outcomes from a recovery protocol for patients with continuous-flow left ventricular assist devices. *J Heart Lung Transplant* 2018 (in press).
- [408] Baldwin AC, Sandoval E, Letsou GV, Mallidi HR, Cohn WE, Frazier OH. Surgical approach to continuous-flow left ventricular assist device explantation: a comparison of outcomes. *J Thorac Cardiovasc Surg* 2016;151:192–8.
- [409] MacGowan GA, Wrightson N, Robinson-Smith N, Woods A, Parry G, Gould K *et al.* Myocardial recovery strategy with decommissioning for the HeartWare left ventricular assist device. *ASAIO J* 2017;63:299–304.
- [410] Segura AM, Radovancevic R, Demirozu ZT, Frazier OH, Buja LM. Granulomatous myocarditis in severe heart failure patients undergoing implantation of a left ventricular assist device. *Cardiovasc Pathol* 2014;23:17–20.
- [411] Roberts WC, Vowels TJ, Ko JM, Capehart JE, Hall SA. Cardiac transplantation for cardiac sarcoidosis with initial diagnosis by examination of the left ventricular apical “core” excised for insertion of a left ventricular assist device for severe chronic heart failure. *Am J Cardiol* 2009;103:110–14.
- [412] Maybaum S, Mancini D, Xydias S, Starling RC, Aaronson K, Pagani FD *et al.* Cardiac improvement during mechanical circulatory support—a prospective multicenter study of the LVAD working group. *Circulation* 2007;115:2497–505.
- [413] Patel SR, Saeed O, Murthy S, Bhatia V, Shin JJ, Wang D *et al.* Combining neurohormonal blockade with continuous-flow left ventricular assist device support for myocardial recovery: a single-arm prospective study. *J Heart Lung Transplant* 2013;32:305–12.
- [414] Selzman CH, Madden JL, Healy AH, McKellar SH, Koliopoulou A, Stehlik J *et al.* Bridge to removal: a paradigm shift for left ventricular assist device therapy. *Ann Thorac Surg* 2015;99:360–7.
- [415] Liang H, Lin H, Weng Y, Dandel M, Hetzer R. Prediction of cardiac function after weaning from ventricular assist devices. *J Thorac Cardiovasc Surg* 2005;130:1555–60.
- [416] Kormos RL, McCall M, Althouse A, Lagazzi L, Schaub R, Kormos MA *et al.* Left ventricular assist device malfunctions: it is more than just the pump. *Circulation* 2017;136:1714–25.
- [417] Potapov EV, Kaufmann F, Stepanenko A, Hening E, Vierecke J, Low A *et al.* Pump exchange for cable damage in patients supported with HeartMate II left ventricular assist device. *ASAIO J* 2012;58:578–82.
- [418] Cubillo EI 4th, Weis RA, Ramakrishna H. Emergent reconnection of a transected left ventricular assist device driveline. *J Emerg Med* 2014;47:546–51.
- [419] Duero Posada JG, Moayedi Y, Alhussein M, Rodger M, Alvarez J, Wintersperger BJ *et al.* Outflow graft occlusion of the heartmate 3 left ventricular assist device. *Circ Heart Fail* 2017;10:1–3.
- [420] Potapov EV, Netuka I, Kaufmann F, Falk V, Mehra MR. Strategy for surgical correction and mitigation of outflow graft twist with a centrifugal-flow left ventricular assist system. *J Heart Lung Transplant* 2018;37:670–3.
- [421] Uriel N, Morrison KA, Garan AR, Kato TS, Yuzefpolskaya M, Latif F *et al.* Development of a novel echocardiography ramp test for speed optimization and diagnosis of device thrombosis in continuous-flow left ventricular assist devices: the Columbia ramp study. *J Am Coll Cardiol* 2012;60:1764–75.
- [422] Scandroglio AM, Kaufmann F, Pieri M, Kretschmar A, Muller M, Pergantis P *et al.* Diagnosis and treatment algorithm for blood flow obstructions in patients with left ventricular assist device. *J Am Coll Cardiol* 2016;67:2758–68.
- [423] Uriel N, Levin AP, Sayer GT, Mody KP, Thomas SS, Adaty S *et al.* Left ventricular decompression during speed optimization ramps in patients supported by continuous-flow left ventricular assist devices: device-specific performance characteristics and impact on diagnostic algorithms. *J Card Fail* 2015;21:785–91.
- [424] Luc JGY, Tchanchaleishvili V, Phan K, Dunlay SM, Maltais S, Stulak JM. Medical therapy compared with surgical device exchange for left ventricular assist device thrombosis: a systematic review and meta-analysis. *ASAIO J* 2018 (in press).
- [425] Centofanti P, Baronetto A, Attisani M, Ricci D, Simonato E, La Torre MW *et al.* Thrombosis in left ventricular assistance device with centrifugal technology: is early thrombolysis a better solution? *Int J Artif Organs* 2017;40:629–35.
- [426] Stulak JM, Dunlay SM, Sharma S, Haglund NA, Davis MB, Cowger J *et al.* Treatment of device thrombus in the HeartWare HVAD: success and outcomes depend significantly on the initial treatment strategy. *J Heart Lung Transplant* 2015;34:1535–41.
- [427] Hanke JS, ElSherbini A, Rojas SV, Avsar M, Shrestha M, Schmitto JD. Aortic outflow graft stenting in patient with left ventricular assist device outflow graft thrombosis. *Artif Organs* 2016;40:414–16.
- [428] Goldstein DJ, Aaronson KD, Tatooles AJ, Silvestry SC, Jeevanandam V, Gordon R *et al.* Gastrointestinal bleeding in recipients of the HeartWare ventricular assist system. *JACC Heart Fail* 2015;3:303–13.
- [429] Dakik HK, McGhan AA, Chiu ST, Patel CB, Milano CA, Rogers JG *et al.* The diagnostic yield of repeated endoscopic evaluation in patients with gastrointestinal bleeding and left ventricular assist devices. *Dig Dis Sci* 2016;61:1603–10.
- [430] Rennyson SL, Shah KB, Tang DG, Kasirajan V, Pedram S, Cahoon W *et al.* Octreotide for left ventricular assist device-related gastrointestinal hemorrhage: can we stop the bleeding? *ASAIO J* 2013;59:450–1.
- [431] Coutance G, Saplan V, Belin A, Repesse Y, Buklas D, Massetti M. Octreotide for recurrent intestinal bleeding due to ventricular assist device. *Asian Cardiovasc Thorac Ann* 2014;22:350–2.
- [432] Katz JN, Adamson RM, John R, Tatooles A, Sundareswaran K, Kalle F *et al.* Safety of reduced anti-thrombotic strategies in HeartMate II patients: a one-year analysis of the US-TRACE Study. *J Heart Lung Transplant* 2015;34:1542–8.
- [433] Teuteberg JJ, Slaughter MS, Rogers JG, McGee EC, Pagani FD, Gordon R *et al.* The HVAD left ventricular assist device: risk factors for neurological events and risk mitigation strategies. *JACC Heart Fail* 2015;3:818–28.
- [434] Nassif ME, Tibrewala A, Raymer DS, Andruska A, Novak E, Vader JM *et al.* Systolic blood pressure on discharge after left ventricular assist

- device insertion is associated with subsequent stroke. *J Heart Lung Transplant* 2015;34:503–8.
- [435] Garan AR, Levin AP, Topkara V, Thomas SS, Yuzefpolskaya M, Colombo PC *et al.* Early post-operative ventricular arrhythmias in patients with continuous-flow left ventricular assist devices. *J Heart Lung Transplant* 2015;34:1611–16.
- [436] Baldwin ACW, Gemmato CJ, Sandoval E, Cohn WE, Morgan JA, Frazier OH. Tolerance of sustained ventricular fibrillation during continuous-flow left ventricular assist device support. *Tex Heart Inst J* 2017;44:357–60.
- [437] Garan AR, Yuzefpolskaya M, Colombo PC, Morrow JP, Te-Frey R, Dano D *et al.* Ventricular arrhythmias and implantable cardioverter-defibrillator therapy in patients with continuous-flow left ventricular assist devices: need for primary prevention? *J Am Coll Cardiol* 2013;61:2542–50.
- [438] Cantillon DJ, Tarakji KG, Kumbhani DJ, Smedira NG, Starling RC, Wilkoff BL. Improved survival among ventricular assist device recipients with a concomitant implantable cardioverter-defibrillator. *Heart Rhythm* 2010;7:466–71.
- [439] Stulak JM, Schettle S, Haglund N, Dunlay S, Cowger J, Shah P *et al.* Percutaneous driveline fracture after implantation of the heartmate ii left ventricular assist device: how durable is driveline repair? *ASAIO J* 2017;63:542–5.
- [440] Goldstein DJ, John R, Salerno C, Silvestry S, Moazami N, Horstmanshof D *et al.* Algorithm for the diagnosis and management of suspected pump thrombus. *J Heart Lung Transplant* 2013;32:667–70.
- [441] Bartoli CR, Ghotra AS, Pachika AR, Birks EJ, McCants KC. Hematologic markers better predict left ventricular assist device thrombosis than echocardiographic or pump parameters. *Thorac Cardiovasc Surg* 2014;62:414–18.
- [442] Potapov EV, Krabatsch T, Buz S, Falk V, Kempfert J. Cerebral protection system applied during washout of thrombus occluding inflow cannula of HeartWare HVAD left ventricular assist device. *J Heart Lung Transplant* 2015;34:1640–1.
- [443] Hubbert L, Forssell C, Baranowski J, Lindgren B, Holm J, Ahn H. Endovascular stenting of a LVAD outflow graft thrombosis. *ASAIO J* 2017;63:e3–5.
- [444] Kemaloglu C, Altekin RE, Bayezid O. First successful percutaneous treatment of a totally occluded HeartWare outflow graft: case report and literature review. *Anatol J Cardiol* 2018;19:341–5.
- [445] Wiedemann D, Schloghofer T, Haberl T, Riebandt J, Dimitrov K, Schima H *et al.* Interventional treatment of LVAD outflow graft stenosis by introduction of bare metal stents. *ASAIO J* 2018;64:e3–7.
- [446] Bhamidipati CM, Pal JD, Jones TK, McCabe JM, Reisman M, Smith JW *et al.* Outflow graft obstruction treated with transcatheter management: a novel therapy for a new diagnosis. *Ann Thorac Surg* 2017;103:e101–4.
- [447] Linneweber J, Dohmen PM, Kerzcher U, Affeld K, Nosé Y, Konertz W. The effect of surface roughness on activation of the coagulation system and platelet adhesion in rotary blood pumps. *Artif Organs* 2007;31:345–51.
- [448] Heilmann C, Trummer G, Beyersdorf F, Brehm K, Berchtold-Herz M, Schelling J *et al.* Acquired Von Willebrand syndrome in patients on long-term support with HeartMate II. *Eur J Cardiothorac Surg* 2017;51:587–90.
- [449] Geisen U, Heilmann C, Beyersdorf F, Benk C, Berchtold-Herz M, Schlensak C *et al.* Non-surgical bleeding in patients with ventricular assist devices could be explained by acquired von Willebrand disease. *Eur J Cardiothorac Surg* 2008;33:679–84.
- [450] Powers WJ, Rabinstein AA, Ackerson T, Adeoye OM, Bambakidis NC, Becker K *et al.* 2018 Guidelines for the early management of patients with acute ischemic stroke: a guideline for healthcare professionals from the American Heart Association/American Stroke Association. *Stroke* 2018;49:e46–110.
- [451] Rimsans J, Levesque A, Lyons E, Sylvester K, Givertz MM, Mehra MR *et al.* Four factor prothrombin complex concentrate for warfarin reversal in patients with left ventricular assist devices. *J Thromb Thrombolysis* 2018;46:180–5.
- [452] Willey JZ, Gavalas MV, Trinh PN, Yuzefpolskaya M, Reshad Garan A, Levin AP *et al.* Outcomes after stroke complicating left ventricular assist device. *J Heart Lung Transplant* 2016;35:1003–9.
- [453] Clerkin KJ, Topkara VK, Mancini DM, Yuzefpolskaya M, Demmer RT, Dizon JM *et al.* The role of implantable cardioverter defibrillators in patients bridged to transplantation with a continuous-flow left ventricular assist device: a propensity score matched analysis. *J Heart Lung Transplant* 2017;36:633–9.
- [454] Soleimani B, Haouzi A, Manoskey A, Stephenson ER, El-Banayosy A, Pae WE. Development of aortic insufficiency in patients supported with continuous flow left ventricular assist devices. *ASAIO J* 2012;58:326–9.
- [455] Saito T, Wassilew K, Gorodetski B, Stein J, Falk V, Krabatsch T *et al.* Aortic valve pathology in patients supported by continuous-flow left ventricular assist device. *Circ J* 2016;80:1371–7.
- [456] Gasparovic H, Kopjar T, Saeed D, Cikes M, Svetina L, Petricevic M *et al.* De novo aortic regurgitation after continuous-flow left ventricular assist device implantation. *Ann Thorac Surg* 2017;104:704–11.
- [457] Atkins BZ, Hashmi ZA, Ganapathi AM, Harrison JK, Hughes GC, Rogers JG *et al.* Surgical correction of aortic valve insufficiency after left ventricular assist device implantation. *J Thorac Cardiovasc Surg* 2013;146:1247–52.
- [458] Parikh KS, Mehrotra AK, Russo MJ, Lang RM, Anderson A, Jeevanandam V *et al.* Percutaneous transcatheter aortic valve closure successfully treats left ventricular assist device-associated aortic insufficiency and improves cardiac hemodynamics. *JACC Cardiovasc Interv* 2013;6:84–9.
- [459] Russo MJ, Freed BH, Jeevanandam V, Hashmi M, Paul JD, Anderson A *et al.* Percutaneous transcatheter closure of the aortic valve to treat cardiogenic shock in a left ventricular assist device patient with severe aortic insufficiency. *Ann Thorac Surg* 2012;94:985–8.
- [460] Cowger JA, Aaronson KD, Romano MA, Haft J, Pagani FD. Consequences of aortic insufficiency during long-term axial continuous-flow left ventricular assist device support. *J Heart Lung Transplant* 2014;33:1233–40.
- [461] Phan K, Haswell JM, Xu J, Assem Y, Mick SL, Kapadia SR *et al.* Percutaneous transcatheter interventions for aortic insufficiency in continuous-flow left ventricular assist device patients: a systematic review and meta-analysis. *ASAIO J* 2017;63:117–22.
- [462] Cowger J, Pagani FD, Haft JW, Romano MA, Aaronson KD, Kolas TJ. The development of aortic insufficiency in left ventricular assist device-supported patients. *Circ Heart Fail* 2010;3:668–74.
- [463] Sayer G, Sarswat N, Kim GH, Adatya S, Medvedofsky D, Rodgers D *et al.* The hemodynamic effects of aortic insufficiency in patients supported with continuous-flow left ventricular assist devices. *J Card Fail* 2017;23:545–51.
- [464] Retzer EM, Sayer GT, Fedson SE, Nathan S, Jeevanandam V, Friant J *et al.* Predictors of survival following trans-catheter aortic valve closure for left ventricular assist device associated aortic insufficiency. *Catheter Cardiovasc Interv* 2016;87:971–9.
- [465] D'Ancona G, Pasic M, Buz S, Drews T, Dreyse S, Hetzer R *et al.* TAVI for pure aortic valve insufficiency in a patient with a left ventricular assist device. *Ann Thorac Surg* 2012;93:e89–91.
- [466] Santini F, Forni A, Dandale R, Ribichini F, Rossi A, Franchi G *et al.* First successful management of aortic valve insufficiency associated with HeartMate II left ventricular assist device support by transfemoral CoreValve implantation. *JACC Cardiovasc Interv* 2012;5:114.
- [467] Schechter MA, Joseph JT, Krishnamoorthy A, Finet JE, Ganapathi AM, Lodge JF *et al.* Efficacy and durability of central oversewing for treatment of aortic insufficiency in patients with continuous-flow left ventricular assist devices. *J Heart Lung Transplant* 2014;33:937–42.
- [468] Loghmanpour NA, Kormos RL, Kanwar MK, Teuteberg JJ, Murali S, Antaki JF. A Bayesian model to predict right ventricular failure following left ventricular assist device therapy. *JACC Heart Fail* 2016;4:711–21.
- [469] Takeda K, Takayama H, Colombo PC, Yuzefpolskaya M, Fukuhara S, Han J *et al.* Incidence and clinical significance of late right heart failure during continuous-flow left ventricular assist device support. *J Heart Lung Transplant* 2015;34:1024–32.
- [470] Uriel N, Adatya S, Maly J, Kruse E, Rodgers D, Heatley G *et al.* Clinical hemodynamic evaluation of patients implanted with a fully magnetically levitated left ventricular assist device (HeartMate 3). *J Heart Lung Transplant* 2017;36:28–35.
- [471] Tedford RJ, Hemnes AR, Russell SD, Wittstein IS, Mahmud M, Zaiman AL *et al.* PDE5A inhibitor treatment of persistent pulmonary hypertension after mechanical circulatory support. *Circ Heart Fail* 2008;1:213–19.
- [472] Haglund NA, Cox ZL, Lee JT, Song Y, Keebler ME, DiSalvo TG *et al.* Are peripherally inserted central catheters associated with increased risk of adverse events in status 1B patients awaiting transplantation on continuous intravenous milrinone? *J Card Fail* 2014;20:630–7.
- [473] Mermel LA, Allon M, Bouza E, Craven DE, Flynn P, O'Grady NP *et al.* Clinical practice guidelines for the diagnosis and management of intravascular catheter-related infection: 2009 update by the Infectious Diseases Society of America. *Clin Infect Dis* 2009;49:1–45.
- [474] Aslam S, Xie R, Cowger J, Kirklin JK, Chu VH, Schueler S *et al.* Bloodstream infections in mechanical circulatory support device recipients in the International Society of Heart and Lung Transplantation Mechanically Assisted Circulation Support Registry: epidemiology, risk factors, and mortality. *J Heart Lung Transplant* 2018;37:1013–20.



- [475] Hooton TM, Bradley SF, Cardenas DD, Colgan R, Geerlings SE, Rice JC *et al.* Diagnosis, prevention, and treatment of catheter-associated urinary tract infection in adults: 2009 international clinical practice guidelines from the Infectious Diseases Society of America. *Clin Infect Dis* 2010;50:625–63.
- [476] Walker PC, DePestel DD, Miles NA, Malani PN. Surgical infection prophylaxis for left ventricular assist device implantation. *J Card Surg* 2011;26:440–3.
- [477] Kusne S, Danziger-Isakov L, Mooney M, Grossi P, Husain S, Pagani F *et al.* Infection control and prevention practices for mechanical circulatory support: an international survey. *J Heart Lung Transplant* 2013;32:S182.
- [478] Lazar HL, Salm TV, Engelman R, Orgill D, Gordon S. Prevention and management of sternal wound infections. *J Thorac Cardiovasc Surg* 2016;152:962–72.
- [479] Bratzler DW, Dellinger EP, Olsen KM, Perl TM, Auwaerter PG, Bolon MK *et al.* Clinical practice guidelines for antimicrobial prophylaxis in surgery. *Am J Health Syst Pharm* 2013;70:195–283.
- [480] Engelman R, Shahian D, Shemin R, Guy TS, Bratzler D, Edwards F *et al.* The society of thoracic surgeons practice guideline series: antibiotic prophylaxis in cardiac surgery, part II: antibiotic choice. *Ann Thorac Surg* 2007;83:1569–76.
- [481] Sousa-Uva M, Head SJ, Milojevic M, Collet JP, Landoni G, Castella M *et al.* 2017 EACTS Guidelines on perioperative medication in adult cardiac surgery. *Eur J Cardiothorac Surg* 2018;53:5–33.
- [482] O'Grady NP, Alexander M, Burns LA, Dellinger EP, Garland J, Heard SO *et al.* Guidelines for the prevention of intravascular catheter-related infections. *Clin Infect Dis* 2011;52:e162–93.
- [483] Marsteller JA, Sexton JB, Hsu YJ, Hsiao CJ, Holzmueller CG, Pronovost PJ *et al.* A multicenter, phased, cluster-randomized controlled trial to reduce central line-associated bloodstream infections in intensive care units\*. *Crit Care Med* 2012;40:2933–9.
- [484] Platt R, Polk BF, Murdock B, Rosner B. Mortality associated with nosocomial urinary-tract infection. *N Engl J Med* 1982;307:637–42.
- [485] Rustemeyer J, Bremerich A. Necessity of surgical dental foci treatment prior to organ transplantation and heart valve replacement. *Clin Oral Invest* 2007;11:171–4.
- [486] Kallen AJ, Wilson CT, Larson RJ. Perioperative intranasal mupirocin for the prevention of surgical-site infections: systematic review of the literature and meta-analysis. *Infect Control Hosp Epidemiol* 2005;26:916–22.
- [487] Hebert C, Robicsek A. Decolonization therapy in infection control. *Curr Opin Infect Dis* 2010;23:340–5.
- [488] Holman WL, Skinner JL, Waites KB, Benza RL, McGiffin DC, Kirklin JK. Infection during circulatory support with ventricular assist devices. *Ann Thorac Surg* 1999;68:711–16.
- [489] Aslam S, Hernandez M, Thornby J, Zeluff B, Darouiche RO. Risk factors and outcomes of fungal ventricular-assist device infections. *Clin Infect Dis* 2010;50:664–71.
- [490] Classen DC, Evans RS, Pestotnik SL, Horn SD, Menlove RL, Burke JP. The timing of prophylactic administration of antibiotics and the risk of surgical-wound infection. *N Engl J Med* 1992;326:281–6.
- [491] Baronetto A, Centofanti P, Attisani M, Ricci D, Mussa B, Devotini R *et al.* A simple device to secure ventricular assist device driveline and prevent exit-site infection. *Interact CardioVasc Thorac Surg* 2014;18:415–17.
- [492] Barber J, Leslie G. A simple education tool for ventricular assist device patients and their caregivers. *J Cardiovasc Nurs* 2015;30:E1–10.
- [493] Wilson W, Taubert KA, Gewitz M, Lockhart PB, Baddour LM, Levison M *et al.* Prevention of infective endocarditis: guidelines from the American Heart Association: a guideline from the American Heart Association Rheumatic Fever, Endocarditis, and Kawasaki Disease Committee, Council on Cardiovascular Disease in the Young, and the Council on Clinical Cardiology, Council on Cardiovascular Surgery and Anesthesia, and the Quality of Care and Outcomes Research Interdisciplinary Working Group. *Circulation* 2007;116:1736–54.
- [494] Baddour LM, Bettmann MA, Bolger AF, Epstein AE, Ferrieri P, Gerber MA *et al.* Nonvalvular cardiovascular device-related infections. *Circulation* 2003;108:2015–31.
- [495] Carr CM, Jacob J, Park SJ, Karon BL, Williamson EE, Araoz PA. CT of left ventricular assist devices. *Radiographics* 2010;30:429–44.
- [496] Dell'Aquila AM, Mastrobuoni S, Alles S, Wenning C, Henryk W, Schneider SR *et al.* Contributory role of fluorine 18-fluorodeoxyglucose positron emission tomography/computed tomography in the diagnosis and clinical management of infections in patients supported with a continuous-flow left ventricular assist device. *Ann Thorac Surg* 2016;101:87–94; discussion 94.
- [497] Tlili G, Picard F, Pinaquy JB, Domingues-Dos-Santos P, Bordenave L. The usefulness of FDG PET/CT imaging in suspicion of LVAD infection. *J Nucl Cardiol* 2014;21:845–8.
- [498] Slaughter MS, Pagani FD, Rogers JG, Miller LW, Sun B, Russell SD *et al.* Clinical management of continuous-flow left ventricular assist devices in advanced heart failure. *J Heart Lung Transplant* 2010;29:S1–39.
- [499] Pereda D, Conte JV. Left ventricular assist device driveline infections. *Cardiol Clin* 2011;29:515–27.
- [500] Lee CR, Thrasher KA. Difficulties in anticoagulation management during coadministration of warfarin and rifampin. *Pharmacotherapy* 2001;21:1240–6.
- [501] Dew MA, Kormos RL, Winowich S, Nastala CJ, Borovetz HS, Roth LH *et al.* Quality of life outcomes in left ventricular assist system inpatients and outpatients. *ASAIO J* 1999;45:218–25.
- [502] Wordingham SE, McIlvennan CK, Fendler TJ, Behnken AL, Dunlay SM, Kirkpatrick JN *et al.* Palliative care clinicians caring for patients before and after continuous flow-left ventricular assist device. *J Pain Symptom Manage* 2017;54:601–8.
- [503] Warraich HJ, Hernandez AF, Allen LA. How medicine has changed the end of life for patients with cardiovascular disease. *J Am Coll Cardiol* 2017;70:1276–89.
- [504] Bayoumi E, Sheikh F, Groninger H. Palliative care in cardiac transplantation: an evolving model. *Heart Fail Rev* 2017;22:605–10.
- [505] Costanzo MR, Dipchand A, Starling R, Anderson A, Chan M, Desai S *et al.* The International Society of Heart and Lung Transplantation Guidelines for the care of heart transplant recipients. *J Heart Lung Transplant* 2010;29:914–56.
- [506] Jaarsma T, Beattie JM, Ryder M, Rutten FH, McDonagh T, Mohacs P *et al.* Palliative care in heart failure: a position statement from the palliative care workshop of the Heart Failure Association of the European Society of Cardiology. *Eur J Heart Fail* 2009;11:433–43.
- [507] Sinha S, Belcher C, Torke A, Howard J, Caccamo M, Slaven JE *et al.* Development of a protocol for successful palliative care consultation in population of patients receiving mechanical circulatory support. *J Pain Symptom Manage* 2017;54:583–8.
- [508] Rogers JG, Patel CB, Mentz RJ, Granger BB, Steinhauser KE, Fiuzat M *et al.* Palliative care in heart failure: the PAL-HF randomized, controlled clinical trial. *J Am Coll Cardiol* 2017;70:331–41.