European Journal of Cardio-Thoracic Surgery 59 (2021) 12–53
doi:10.1093/ejcts/ezaa283 Advance Access publication 7 October 2020

POSITION STATEMENT

Cite this article as: Lorusso R, Whitman G, Milojevic M, Raffa G, McMullan DM, Boeken U *et al.* 2020 EACTS/ELSO/STS/AATS expert consensus on post-cardiotomy extracorporeal life support in adult patients. Eur J Cardiothorac Surg 2021;59:12–53.

2020 EACTS/ELSO/STS/AATS expert consensus on post-cardiotomy extracorporeal life support in adult patients

Roberto Lorusso [a,*,†] (Chairperson) (Netherlands), Glenn Whitman[b,*,†] (Chairperson) (USA), Milan Milojevic [c,d,e,†] (Serbia, Netherlands), Giuseppe Raffa [f] (Italy), David M. McMullan[g] (USA), Udo Boeken[h] (Germany), Jonathan Haft [i] (USA), Christian A. Bermudez[j] (USA), Ashish S. Shah[k] (USA) and David A. D'Alessandro[l] (USA)

[a] Department of Cardio-Thoracic Surgery, Heart & Vascular Centre, Maastricht University Medical Centre, Cardiovascular Research Institute Maastricht, Maastricht, Netherlands
[b] Cardiovascular Surgery Intensive Care, Johns Hopkins Hospital, Baltimore, MD, USA
[c] Department of Anaesthesiology and Critical Care Medicine, Dedinje Cardiovascular Institute, Belgrade, Serbia
[d] Department of Cardiovascular Research, Dedinje Cardiovascular Institute, Belgrade, Serbia
[e] Department of Cardiothoracic Surgery, Erasmus University Medical Center, Rotterdam, Netherlands
[f] Department for the Treatment and Study of Cardiothoracic Diseases and Cardiothoracic Transplantation, IRCCS-ISMETT (Istituto Mediterraneo per i Trapianti e Terapie ad Alta Specializzazione), Palermo, Italy
[g] Department of Cardiac Surgery, Seattle Children Hospital, Seattle, WA, USA
[h] Department of Cardiac Surgery, Heinrich Heine University, Dusseldorf, Germany
[i] Section of Cardiac Surgery, University of Michigan, Ann Arbor, MI, USA
[j] Department of Cardiovascular Surgery, Hospital of the University of Pennsylvania, Philadelphia, PA, USA
[k] Department of Cardio-Thoracic Surgery, Vanderbilt University Medical Center, Nashville, TN, USA
[l] Department of Cardio-Thoracic Surgery, Massachusetts General Hospital, Boston, MA, USA

EACTS/ELSO/STS/AATS Committee Reviewers: Rakesh Christopher Arora (Canada), Nick Freemantle (UK), Christoph Knosalla (Germany), Graeme Maclaren (Singapore), Evgenij V. Potapov (Germany), Christoph Schmid (Germany), Kiran Shekar (Australia), Scott Silvestri (USA) and Alexander Wahba (Norway)

* Corresponding authors. Department of Cardio-Thoracic Surgery, Heart & Vascular Centre, Maastricht University Medical Centre, Cardiovascular Research Institute Maastricht, Maastricht, Netherlands. Tel: +31-43-3876032; e-mail: roberto.lorusso@mumc.nl (R. Lorusso); Cardiovascular Surgery Intensive Care, Johns Hopkins Hospital, Baltimore, MD, USA. Tel: +1-410-9553285; e-mail: gwhitman@jhmi.edu (G. Whitman).

Received 16 October 2019; received in revised form 3 April 2020; accepted 21 April 2020

[†] These authors contributed equally to this work.

Disclaimer 2020: The EACTS/ELSO/STS/AATS expert consensus represent the views of the EACTS, ELSO, STS and AATS and were produced after careful consideration of the scientific and medical knowledge and the evidence available at the time of their dating. The EACTS, ELSO, STS and AATS are not responsible in the event of any contradiction, discrepancy and/or ambiguity between this document and any other official recommendations or guidelines issued by the relevant public health authorities, in particular in relation to good use of healthcare or therapeutic strategies.

The EACTS, ELSO, STS and AATS expert consensus does not, in any way whatsoever, override the individual responsibility of health professionals to make appropriate and accurate decisions in consideration of each patient's health condition and, where appropriate and/or necessary, in consultation with that patient and the patient's care provider. Nor do the EACTS, ELSO, STS and AATS expert consensus exempt health professionals from giving full and careful consideration to the relevant official, updated recommendations or guidelines issued by the competent public health authorities, in order to manage each patient's case in light of the scientifically accepted data pursuant to their respective ethical and professional obligations. It is also the health professional's responsibility to verify the applicable rules and regulations relating to drugs and medical devices at the time of prescription.

Downloaded from https://academic.oup.com/ejcts/article/59/1/12/5918808 by guest on 08 February 2021

Abstract

Post-cardiotomy extracorporeal life support (PC-ECLS) in adult patients has been used only rarely but recent data have shown a remarkable increase in its use, almost certainly due to improved technology, ease of management, growing familiarity with its capability and decreased costs. Trends in worldwide in-hospital survival, however, rather than improving, have shown a decline in some experiences, likely due to increased use in more complex, critically ill patients rather than to suboptimal management. Nevertheless, PC-ECLS is proving to be a valuable resource for temporary cardiocirculatory and respiratory support in patients who would otherwise most likely die. Because a comprehensive review of PC-ECLS might be of use for the practitioner, and possibly improve patient management in this setting, the authors have attempted to create a concise, comprehensive and relevant analysis of all aspects related to PC-ECLS, with a particular emphasis on indications, technique, management and avoidance of complications, appraisal of new approaches and ethics, education and training.

Keywords: Guidelines • Consensus statements • Cardiac surgery • Postcardiotomy failure • Extracorporeal life support • Extracorporeal membrane oxygenation • Mechanical support

REPORT

Downloaded from https://academic.oup.com/ejcts/article/59/1/12/5918808 by guest on 08 February 2021

TABLE OF CONTENTS

ABBREVIATIONS AND ACRONYMS 14
1. PREAMBLE 14
2. METHODS 14
3. INTRODUCTION AND TERMINOLOGY 15
4. EPIDEMIOLOGY AND PATIENT PROFILES 15
4.1 Background 15
4.2 Evidence review 16
4.3 Preoperative patient profile and peculiarities of post-cardiotomy extracorporeal life support 16
5. INDICATIONS, CONTRAINDICATIONS AND PROGNOSTICATION 17
5.1 Clinical presentation and initial severity assessment . . 17
5.2 Indications 17
5.3 Contraindications 18
5.4 Prognostication 18
5.5 Areas of uncertainty 8
6. EXTRACORPOREAL LIFE SUPPORT FUNDAMENTALS AND DETAILS 19
6.1 Background 19
6.2 Centrifugal pumps 19
6.3 Oxygenators 19
6.4 Circuitry integration 19
6.5 Extracorporeal life support flow 20
6.6 Gas management 20
6.7 Description of evidence 20
7. EXTRACORPOREAL LIFE SUPPORT MODE AND CONFIGURATIONS 21
7.1 Background 21
7.2 Evidence review 21
7.3 Extracorporeal life support for isolated right ventricular failure 22
7.4 Hybrid extracorporeal life support configurations 22
7.5 Combinations of devices 23
8. INTRA-AORTIC BALLOON PUMP AND CONCOMITANT CARDIOCIRCULATORY ASSISTANCE ALTERNATIVES . . 23
8.1 Introduction 23
8.2 Intra-aortic balloon pump and alternate short-term mechanical circulatory support platforms 23
8.3 Evidence review 24
8.3.1 Intra-aortic balloon pump 24
8.3.2 Impella 24
8.3.3 TandemHeart 24
8.3.4 Short-term ventricular assist devices 24
9. IMPLANT 25
9.1 Background 25
9.2 Evidence review 25
9.2.1 Timing and location 25
9.2.2 Cannulation 25
9.2.3 Left heart venting 26
10. MANAGEMENT OF INITIATION OF INTRAOPERATIVE EXTRACORPOREAL LIFE SUPPORT 29
10.1 Sternum management 29
10.2 Inotropes, vasoconstrictors and steroids 30
10.3 Antibiotics 30
10.4 Monitoring during intraoperative extracorporeal life support implant 30
10.4.1 Blood pressure pulsatility 30
10.4.2 Peripheral arterial/pulse oximetry 30
10.4.3 Pulmonary artery catheter 31
10.4.4 Echocardiography 31
10.4.5 Near-infrared spectroscopy 31
10.5 Description of the evidence 32
10.5.1 Peripheral arterial/pulse oximetry 32
10.5.2 Pulmonary artery catheter 32
10.5.3 Echocardiography 32
10.5.4 Cerebral and lower limb near-infrared spectroscopy 32
10.6 Reversal of anticoagulation and the management of major bleeding 32
10.6.1 The evidence 32
11. POSTOPERATIVE ANTICOAGULATION 32
11.1 Background 32
11.1.1 Heparin 32
11.1.2 Direct thrombin inhibitors 33
11.2 The evidence 33
11.2.1 Bleeding 33
11.2.2 Commencement of postoperative anticoagulation 33
11.3 Monitoring of coagulation systems 34
11.3.1 Evidence for monitoring guidelines . . . 34
11.3.2 Heparin-induced thrombocytopaenia . 34
12. INTENSIVE CARE UNIT MANAGEMENT DURING EXTRACORPOREAL LIFE SUPPORT 34
12.1 Haemodynamics 34
12.1.1 Background 34
12.1.2 The evidence 35
12.2 Left ventricular distension 35
12.3 Vascular and system-related complications 35
12.4 Ventilation 35
12.4.1 Background 35

12.4.2 The evidence 36
12.5 Infections 36
12.5.1 Background 36
12.5.2 The evidence 37
12.6 Management of renal function 37
12.6.1 Background 37
12.6.2 The evidence 37
12.7 Central nervous system monitoring 37
12.7.1 Background and evidence 37
12.7.2 Electroencephalography and somatosensory evoked potential 38
12.7.3 Computed tomography imaging 39
12.7.4 Near-infrared spectroscopy 39
12.7.5 Transcranial Doppler 39
13 WEANING, TRANSITION AND OUTCOMES 39
13.1 Weaning modalities and monitoring 39
13.2 Failure to wean, transition to ventricular assist device or heart transplant or termination 40
13.3 Early and long-term results 40
13.3.1 Early results 41
13.3.2 Long-term results 41
14 ETHICS, FAMILY AND FUTILITY 41
14.1 Background 41
14.2 Family relationships 41
14.3 Futility 42
15 EXTRACORPOREAL LIFE SUPPORT EDUCATION AND TRAINING 42
15.1 Background 42
15.2 How to teach extracorporeal life support 42
16 HUB-AND-SPOKE MODEL: TRANSPORT 42
16.1 Hub-and-spoke network 42
16.2 Patient transport 43
17 THE IMPORTANCE OF A MULTIDISCIPLINARY TEAM 32
17.1 Team composition and credentialing 43
17.2 Quality and performance improvement dashboards 43
18 POST-CARDIOTOMY CARDIOPULMONARY RESUSCITATION WITH EXTRACORPOREAL LIFE SUPPORT 44
18.1 Background 44
18.2 Incidence 44
18.3 Setting and organization 44
19 SPECIAL CONDITIONS 44
19.1 Background 44
19.2 Preoperative extracorporeal life support 45
19.3 Prophylactic extracorporeal life support 45
19.4 Veno-venous extracorporeal life support 46
19.5 Post-heart transplant extracorporeal life support (graft failure) 46
19.6 Extracorporeal life support after a left ventricular assist device 46
20 LIMITATIONS 47
21 CONCLUSIONS 47

ABBREVIATIONS AND ACRONYMS

ACT	Activated clotting time
aPTT	Activated partial thromboplastin time
ARDS	Acute respiratory distress syndrome
AT	Antithrombin
CABG	Coronary artery bypass grafting
CO	Cardiac output
CO2	Carbon dioxide
CPB	Cardiopulmonary bypass
DTIs	Direct thrombin inhibitors
EACTS	European Association for Cardio-Thoracic Surgery
ECLS	Extracorporeal life support
ECMO	Extracorporeal membrane oxygenation
ECPR	Extracorporeal cardiopulmonary resuscitation
ELSO	Extracorporeal Life Support Organization
HIT	Heparin-induced thrombocytopaenia
HTx	Heart transplant
IABP	Intra-aortic balloon pump
ICU	Intensive care unit
LCO	Low cardiac output
LT-MCS	Long-term mechanical circulatory support
LV	Left ventricle
LVAD	Left ventricular assist device
MCS	Mechanical circulatory support
MI	Myocardial infarction
Oxy-RVAD	Right ventricular assist device with oxygenator
PA	Pulmonary artery
PC	Post-cardiotomy
PCS	Post-cardiotomy shock
PGD	Primary graft dysfunction
RCT	Randomized controlled trial
RRT	Renal replacement therapy
RV	Right ventricle
RVAD	Right ventricular assist device
SAVE	Survival After Veno-arterial ECMO
ST-MCS	Short-term mechanical circulatory support
STS	Society of Thoracic Surgeons
V-A	Veno-arterial
V-V	Veno-venous

1. PREAMBLE

This document represents a joint effort by the European Association for Cardio-Thoracic Surgery (EACTS), the Extracorporeal Life Support Organization (ELSO), the Society of Thoracic Surgeons (STS) and the American Association for Thoracic Surgery (AATS) to provide a position paper on post-cardiotomy extracorporeal life support (PC-ECLS) in adult patients, the goal of which is to provide comprehensive and useful recommendations about the most relevant issues surrounding its application and to highlight several aspects that deserve attention in order to optimize indications and applications, to suggest configurations, to avoid or manage complications and to improve outcomes in a population of patients who are critically ill and who have an extremely high risk of mortality.

2. METHODS

Members of the 4 societies with significant experience in the field were selected and invited to join the task force by their respective societies, which officially endorsed this scientific and educational initiative. Following the methodological quality assessment across available body of evidence specific recommendations

Downloaded from https://academic.oup.com/ejcts/article/59/1/12/5918808 by guest on 08 February 2021

Table 1: 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	**The consensus of expert opinion and/or small studies, retrospective studies, registries.**

Table 2: 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 and effective.**	**Is recommended/is indicated**
Class II	**Conflicting evidence and/or a divergence of opinion about the usefulness/efficacy of the given treatment or procedure.**	
Class IIa	***Weight of evidence/opinion is in favour of usefulness/efficacy.***	**Should be considered**
Class IIb	***Usefulness/efficacy is less well established by evidence/opinion.***	**May be considered**
Class III	**Evidence/general agreement that the given treatment/procedure is not useful/effective and may sometimes be harmful.**	**Is not recommended**

were developed after careful consideration of the scientific and medical knowledge contained in each article and the evidence available at the time of its writing, following the methods manual for EACTS clinical guidelines [1].

After the scope of the guidelines was agreed upon by the task force members, the table of contents was established, and topics were allocated to writing groups of at least 2 members during a face-to-face meeting. The standardized Population, Intervention, Comparison, Outcome and Time (PICOT) framework was used to facilitate systematic literature review, establishing answerable research questions. The systematic literature search was not restricted in terms of years but was mainly focused on cardiac surgery in adults and did not include studies in languages other than English.

The systematic literature search was performed by the section authors and was also instrumental in identifying a recently published systematic review [2] that received further support from other recognized experts from the worldwide ECLS community. An additional overall complementary literature search was performed by a PhD fellow dedicated to the topic (G.R.) and member of the task force. The medical evidence was critically appraised for quality by a clinical epidemiologist (M.M.).

All chapters were written through a close collaboration between the task force members. Following the official policy for the EACTS clinical guidelines [1], the task force members were asked to complete declarations of interest and write chapters only if they had no disclosures for the specific topic. Agreement on the finalized document and recommendations was reached through conference calls and face-to-face meetings, without excluding members with a conflict of interest. The hierarchy of evidence required by the study design along with the internal hierarchy based on the study quality was used to formulate levels and grades of recommendations. In the absence of published evidence, expert consensus statements were made to cover specific issues that are essential to daily practice. The level of evidence and the strength of the recommendations were weighed and graded according to predefined scales, as outlined in Tables 1 and 2.

3. INTRODUCTION AND TERMINOLOGY

PC-ECLS represents a well-established and valuable tool to rescue patients in refractory cardiocirculatory failure, with or without concomitant respiratory dysfunction, in various circumstances that otherwise would almost certainly lead to death. Although PC-ECLS has been in use since the early 1970s, its application has witnessed a recent resurgence in the adult setting during the last 2 decades, particularly in cardiac surgery [3, 4]. Technological advances, increased expertise, availability, ease of application and management and more affordable costs [a fraction of the cost of implantable mechanical circulatory support (MCS)] have been responsible for its broader use.

The increased use of PC-ECLS, however, has been paralleled by continued disappointing outcomes, characterized by high morbidity and mortality [5]. PC-ECLS is an aggressive, resource-intensive and clinically demanding procedure, in which a multidisciplinary approach and sophisticated expertise are of paramount importance and need to exist universally if we are to improve on current results [6].

Furthermore, although the need for PC-ECLS may be unexpected and required for unforeseen intraoperative or postoperative adverse events, in many situations it may be a predictable event, allowing for its timely, post-bypass use, thereby avoiding irreversible injury to a patient who otherwise would experience cardiac, respiratory or cardiorespiratory failure. Patient selection, timely application, the presence of educated and well-trained ECLS users, use of adequate precautions and implantation principles, periprocedural ECLS management, use of a well-established weaning protocol and recognition of futility with the need for cessation of therapy or the need for even more advanced therapies, represent significant components in the use of PC-ECLS that theoretically could improve success in this high-risk population of patients.

The goal of this position paper was to identify the most important aspects of adult PC-ECLS and provide a useful vade mecum for daily patient decision-making and management (Supplementary Material, Tables S1–S3).

This document refers to the ECLS-related terminology included in a recent paper (modified from Broman *et al.* [7] released by ELSO (Table 3). Furthermore, this document accounts for and addresses ECLS as extracorporeal life support with an oxygenator, also known as extracorporeal membrane oxygenation (ECMO). Other temporary cardiocirculatory support is described as short-term mechanical circulatory support (ST-MCS) or long-term mechanical circulatory support (LT-MCS) [8].

4. EPIDEMIOLOGY AND PATIENT PROFILES

4.1 Background

The use of ECLS is increasing dramatically for acute cardiocirculatory compromises, e.g. refractory cardiac arrest, acute pulmonary embolism, severe cardiogenic shock after acute myocardial infarction (MI), as well as other categories of acute cardiac failure unresponsive to conventional aggressive treatments [3, 4].

REPORT

Downloaded from https://academic.oup.com/ejcts/article/59/1/12/5918808 by guest on 08 February 2021

Table 3: Nomenclature of ECLS modes and configurations

ECLS	• A collective term for extracorporeal therapies used for the support of various presentations of cardiac and/or pulmonary failure through the use of an ECC • ECLS includes therapies focusing on oxygenation, CO_2 removal, cardiac support or a combination thereof. It excludes ECC for cardiothoracic or vascular surgical procedures
ECMO	• ECMO is the provision of O_2 and CO_2 exchange through the use of an extracorporeal circuit consisting minimally of a blood pump, artificial lung and vascular access cannula, using blood flows sufficient to support oxygenation and concomitantly enhance CO_2 removal • The term ECLS has been used interchangeably with the term ECMO, but ECMO is most commonly used when the goal is only O_2 delivery and CO_2 exchange by means of a pumped extracorporeal circuit
VA support	• V-A support is the application of ECC primarily for cardiocirculatory or cardiopulmonary support, in which the extracorporeal circuit drains blood from the venous system and returns it to the systemic arterial system oxygenated and normalized for pCO_2. Without qualification, V-A support refers to support that returns blood to the systemic arterial system, operating in parallel with and providing partial or complete bypass of the heart and lungs. Although used primarily for cardiac support, in selected circumstances, V-A support is used for respiratory or combined cardiac and respiratory support • V-A can be used to qualify the application of ECLS (V-A ECLS)
VV support	• V-V support is the application of ECLS primarily for respiratory support, in which the extracorporeal circuit drains blood from the venous system and reinfuses it into the venous system. V-V support operates in series with the heart and lungs and does not provide a bypass of these organs • V-V can be used to qualify the application of ECLS (V-V ECLS). Variations of V-V support include a) the use of a dual-lumen cannula inserted across the tricuspid valve into the pulmonary artery that supports RV function in addition to gas exchange (also called Oxy-RVAD) or b) other configurations (a right atriopulmonary or right-to-left atrium connection with pump and oxygenators can be considered if isolated lung dysfunction occurs)
V-VA support	• V-VA is a hybrid configuration of V-V and V-A extracorporeal support in which the ECLS circuit drains blood from the venous system and reinfuses it into both the venous and systemic arterial systems. V-VA ECLS provides both pulmonary (V-V component) and cardiac (V-A component) support in patients with combined cardiopulmonary failure • Other ECLS configurations are possible (called hybrid ECLS) and provided in document released by ELSO [7] • V-VA can be used to qualify the application of ECMO (V-VA ECLS). The abbreviation V-VA is preferred over V-AV since it is a contraction of 'V-V' and 'V-A' and is established in the literature
ECPR	• ECPR is the application of rapid-deployment V-A ECLS, usually by peripheral cannulation, to provide circulatory support in patients in whom conventional CPR is unsuccessful in achieving a sustained ROSC. Sustained ROSC is deemed to have occurred when chest compressions are not required for 20 consecutive min and signs of circulation persist • ECPR implies the application of ECLS during conventional CPR. Use of ECLS initiated for LCO following sustained ROSC is considered V-A ECMO, not ECPR
Prolonged ECLS	A continuous episode of ECLS for more than 7–10 days for cardiac ECLS and more than 28 days for respiratory ECLS. It does not indicate the type or mode of ECLS

CO_2: carbon dioxide; CPR: cardiopulmonary resuscitation; ECC: extracorporeal circulation; ECLS: extracorporeal life support; ECMO: extracorporeal membrane oxygenation; ECPR: extracorporeal cardiopulmonary resuscitation; ELSO: Extracorporeal Life Support Organization; LCO: low cardiac output; LV: left ventricular; O_2: oxygen; Oxy-RVAD: right ventricular assist device with oxygenator; ROSC: return of spontaneous circulation; RV: right ventricular; V-AV: veno-arterialvenous; V-VA: veno-venousarterial; VA: veno-arterial; VV: veno-venous.

Furthermore, it is rapidly becoming an essential therapy for supporting patients experiencing acute cardiocirculatory compromise intraoperatively, preoperatively or postoperatively [4, 5].

As previously mentioned, several factors have promoted the application of PC-ECLS [3, 5], along with other circulatory assist devices proposed for use in this setting [9, 10].

This document attempts to provide the reader with a current assessment of PC-ECLS, as a useful tool to help the practitioner fully understand its current strengths and limitations as well as those human factors that are a prerequisite for successful outcomes. Alternative approaches to caring for this patient population are briefly touched upon.

4.2 Evidence review

Information about the use of perioperative ECLS in cardiac surgery is limited. Indeed, few robust patient series (>50 cases) on its use have been reported in the last 25 years [11, 12]. Prevalence of its application ranges from 0.3% to 3.6% [2, 11, 12], highlighting its limited but highly variable use in this setting. Although several national and international surveys have confirmed an increase in the use of ECLS in surgical subjects [3, 4], an analysis of the ELSO Registry reveals a parallel steady decline in the number of survivors [5].

Although PC-ECLS is decreasing as a percentage of all adult ECLS cases, this decrease is the result of the increased application of ECLS for the treatment of non-surgical cardiogenic shock and refractory cardiac arrest. However, because the absolute number of cases of PC-ECLS is increasing, it continues to be the most common cardiac application of ECLS in adult patients [13].

4.3 Preoperative patient profile and peculiarities of post-cardiotomy extracorporeal life support

Patient characteristics potentially associated with the use of PC-ECLS have been investigated, but no clearly defined profiles have

Downloaded from https://academic.oup.com/ejcts/article/59/1/112/5918808 by guest on 08 February 2021

REPORT

been identified. Relatively young patient age (<60 years), preoperative renal insufficiency, prior MI, the presence of left-main disease, left ventricular (LV) dysfunction, prolonged history of coronary artery disease with previous MI, prior open-heart surgery and urgent or emergent status, all characterize the PC-ECLS patient [14]. Patient age represents a controversial aspect of PC-ECLS. Several centres deny access to ECLS for patients above a cut-off age, whereas the majority regard older age as only a relative contraindication [15, 16].

As expected, due to procedural volumes, the most frequent subgroup of patients on PC-ECLS is represented by those who have coronary artery bypass grafting (CABG), followed by valve surgery, associated valve/coronary surgery and others [2]. It is noteworthy that despite previously being considered an absolute contraindication, PC-ECLS, post-repair of acute aortic dissection is no longer a contraindication. PC-ECLS may provide effective assistance in patients prior to and after heart transplantation (HTx) or left ventricular assist device (LVAD) implantation [2]. ECLS is used in as many as 10–15% of patients after HTx or LVAD, thereby representing an invaluable tool in such settings [17, 18]. The use of marginal donor hearts, although predisposing to the need for temporary support, may improve the donor pool size. The use of ECLS apparently does not influence primary graft recovery or patient survival to discharge [19]. After LVAD implantation, right ventricular (RV) failure occurs in as many as 25% of the supported patients, often requiring mechanical support regardless of type [20, 21]. Indeed, PC-ECLS is increasingly considered in this setting to support the RV while it recovers or as a bridge to decision regarding the need for an RV assist device (RVAD) [21, 22].

The use of ECLS for PC cardiac arrest has been considered more frequently during the last 10 years, with a constant increase over time [23] and with promising results as reflected by the latest 2017 STS Expert Consensus for the Resuscitation of Patients Who Arrest After Cardiac Surgery [24].

In PC-ECLS, the caregivers face specific comorbidities and conditions that distinguish the PC-ECLS candidate and that influence patient management and outcome (Fig. 1).

5. INDICATIONS, CONTRAINDICATIONS AND PROGNOSTICATION

5.1 Clinical presentation and initial severity assessment

PC failure remains an infrequent complication that occurs in <4% of adult patients undergoing cardiac surgery [2, 25]. The precise definition of PC cardiac failure is generally understood as an inability to separate from cardiopulmonary bypass (CPB) or persistent cardiogenic shock despite maximal use of pharmacological agents. What often clouds the clinical picture is the fact that many patients during initial weaning from CPB may transiently demonstrate poor ventricular function and low cardiac output (LCO) that resolves quickly with pharmacological optimization. The challenge is determining who will not rapidly recover and, thus, will benefit from immediate initiation of mechanical support thereby preventing the detrimental effects of delay in providing circulatory support. In making this determination, one must consider the following factors: patient comorbidities, the degree and trajectory of post-bypass myocardial dysfunction, satisfaction with the procedure just performed, including whether myocardial recovery was optimized, ongoing bleeding concerns, and any preoperative discussions that may have taken place regarding the patient's wishes for aggressive support. In addition, timely implantation prior to severe end-organ hypoperfusion and ischaemic injury represents one of the most powerful predictors of ECLS outcome, as discussed later in this document. Therefore, if maximal pharmacological support and, despite recent controversies, intra-aortic balloon pump (IABP) assistance prove unsuccessful, ECLS should be instituted in the presence of unresponsive LCOS due to uni- or biventricular failure during or after CPB, at the earliest signs of end-organ injury, or at the onset of anaerobic metabolism where pharmacological management is unlikely to be effective. Prophylactic application may be considered in particular circumstances, as discussed in Section 19.

Several scoring systems are currently used to prognosticate outcomes in critically ill patients. The APACHE (Acute Physiology, Age, Chronic Health Evaluation) score incorporates a variety of physiological parameters, laboratory values, chronic illness, intensive care unit (ICU) admission diagnosis and age [26]. Although it has been validated in the general ICU population, this system specifically excludes PC patients. The SAVE (Survival After Veno-arterial ECMO) score was created specifically for adult patients supported by veno-arterial (VA) ECLS, as indicated in the ELSO registry [27]. Because it incorporates physiological and diagnostic variables prior to ECLS, the SAVE score performed better than all other scoring tools in an independent validation cohort. However, as with APACHE [27], the SAVE score was not designed for the PC shock (PCS) population, because it does not account for the unique alterations in physiology for the patients on CPB. The REMEMBER (pRedicting mortality in patients undergoing veno-arterial Extracorporeal MEMBrane oxygenation after coronary artEry bypass gRafting) score was developed from a PC cohort but was limited to those undergoing isolated CABG [28]. This score performed better than the SAVE score in their validation cohorts but was derived from a single institution and may not be generalizable. Clearly, more work is necessary to create reliable risk predictive models (Supplementary Material, Fig. S1) across multiple centres in a mixed PC population to more accurately predict survival for those in whom PC-ECLS is being considered.

5.2 Indications

As described previously, the indications for PC-ECLS are persistent cardiogenic shock despite optimal inotropic support following cardiac surgery procedures. Currently there is no consensus regarding when to initiate ECLS in this setting. Furthermore, the previously described scoring models were developed in those patients who received ECLS without including the larger denominator in which ECLS may have been considered. The IABP-SHOCK risk score was developed out of the Intra-Aortic Balloon Pump in Cardiogenic Shock randomized controlled trial (RCT) to predict death in the setting of acute MI [29]. Although some of the elements incorporated in that model may be transferrable to the PC population, there are certain variables unique to cardiac surgical patients that would be important to consider. The most simplistic and relevant predictor of death PC was described by Samuels *et al.* in a classic paper [30]. It relies on the number of high-dose inotropes necessary to initially separate from CPB as a predictor of mortality. This study forms the basis for the indications for ECLS early in the PC

Downloaded from https://academic.oup.com/ejcts/article/59/1/12/5918808 by guest on 08 February 2021

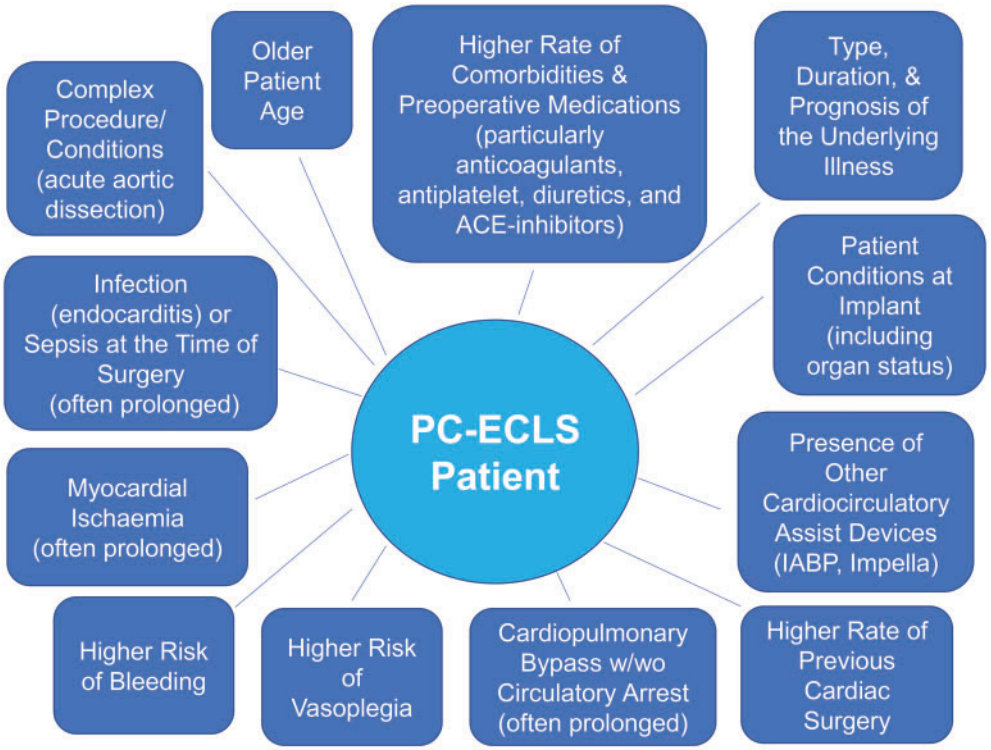

Figure 1: Characteristics of the PC-ECLS patient that, in many instances, differ from those of other potential recipients and clinical settings, all of which impact outcome. ACEI: angiotensin-converting enzyme inhibitors; IABP: intra-aortic balloon pump; PC-ECLS: post-cardiotomy extracorporeal life support.

setting. Almost certainly because of a lack of strong predictive evidence, significant variability remains in the use of 'multiple inotropes' as the indication for PC-ECLS. Clearly, though, the decision to institute ECLS is based on the risks and benefits of high-dose inotropes and LCO compared to ECLS with its associated complications and challenges.

Recognition of the variety of approaches to MCS is discussed in Sections 7 and 19.

5.3 Contraindications

The only absolute contraindication to PC-ECLS support is uncontrollable bleeding. All other contraindications are relative and the goals of treatment must be considered. For patients in whom myocardial recovery is felt to be unlikely, ECLS should only be initiated if the patient appears to be a candidate for advanced cardiac therapy, e.g. LT-MCS or HTx. These criteria would typically exclude patients with preoperative chronic organ failure or advanced age. For patients in whom PC failure is felt to be reversible, all contraindications are relative. The presence of comorbidities likely to impact the immediate perioperative period, including pre-existing end-stage or advanced lung, liver and renal disease are relative contraindications. Severe peripheral vascular disease and known cerebral vascular disease also represent barriers to short- and long-term recovery, as they increase the risk of perioperative complications. Aortic valve insufficiency, although not an absolute contraindication, should be addressed either surgically or via transcatheter techniques if, supported by V-A ECLS, significant valve regurgitation is present (greater than grade 2 and with signs of LV distension). Even mild aortic regurgitation might lead to a degree of LV distension with V-A ECLS, which may delay recovery and lead to respiratory compromise. Some form of ventricular venting may be beneficial in this setting and is discussed elsewhere in this document.

5.4 Prognostication

In addition to the SAVE and REMEMBER scores described previously, there are abundant data characterizing survival during PC-ECLS. Large single-centre reports demonstrated survival from 25% to 42%, with end-organ injury and lactate levels predictive of mortality [31, 32]. In a recent large meta-analysis, survival to discharge was 34%, and age and pre-ECLS lactate levels appeared to be important consistent predictors of outcome [33]. What may be more important than the initial absolute value of the lactate level is lactate clearance during the initial period of support [34]. Prognostication after an IABP implant in patients with PCS has been described and may be useful in characterizing patients at higher risk for subsequent further deterioration that requires more aggressive circulatory support and, therefore, a timely ECLS implant, such as patients with elevated left atrial pressure, low mixed venous oxygen saturation and other markers of peripheral hypoperfusion due to refractory LCOS despite adequate pharmacological treatment [35]. Despite the poor outcomes experienced, without PC-ECLS, survival of these patients may be close to zero.

Clearly, the ability to prognosticate is essential not only for the selection of appropriate candidates for ECLS, but equally to reliably predict futility, which would prompt ECLS termination.

Downloaded from https://academic.oup.com/ejcts/article/59/1/12/5918808 by guest on 08 February 2021

5.5 Areas of uncertainty

Increased age certainly has been associated with worse outcomes, however, there is no absolute contraindication to using PC-ECLS in older adults. Although patients in their 80s have been supported with success, there needs to be careful thought to appropriate selection of these patients because they will not be candidates for a durable LVAD or HTx. They must be patients in whom myocardial recovery is reasonably likely. The impact of preoperative frailty on survival after ECLS has also not been formally evaluated. It is reasonable to assume that frail patients, by definition, lack physiological reserve and therefore are particularly at risk for complications and subsequent death on ECLS. This possibility also should be considered when unexpected postoperative myocardial failure is encountered.

Recommendations for indications, contraindications and prognostication of PC-ECLS

Recommendations	Class[a]	Level[b]
It is recommended that PC support be initiated prior to end-organ injury or onset of anaerobic metabolism (lactate level <4 mmol/l) in patients with likelihood of myocardial recovery and in the absence of uncontrollable bleeding not amenable to surgical repair. [14, 33].	I	B
When the likelihood of native myocardial recovery is low, PC ECLS is recommended in patients who are eligible for LT-MCS or a HTx.	I	C
The early use of ECLS after cardiac surgery in a patient with an IABP and optimal medical therapy, with failure to wean from CPB or marginal haemodynamics is recommended [33].	I	B
Significant comorbidities, advanced age, elevated lactate level and renal injury are risk factors associated with death and should be considered prior to ECLS initiation [27, 25, 33].	IIa	B
Preoperative implant of ECLS may be considered in patients in very poor condition (haemodynamic or metabolic) or with structural cardiac anomalies (postacute MI VSD, severe lung oedema or dysfunction due to underlying cardiac disease) to facilitate perioperative management (bridge to surgery).	IIb	C
It should be considered that the type and modality of ECLS (uni or biventricular failure, right or left ventricular compromise, preoperative, intraoperative or postoperative cardiocirculatory failure, acute or chronic cardiac dysfunction, cardiogenic shock or cardiac arrest, including alternative mechanical support device) are discussed based on the type of haemodynamic condition and patient characteristics.	IIa	C

[a]Class of recommendation.
[b]Level of evidence.
CPB: cardiopulmonary bypass; ECLS: extracorporeal life support; HTx: heart transplant; IABP: intra-aortic balloon pump; LT-MCS: long-term mechanical circulatory support; MI: myocardial infarction; PC: post-cardiotomy; VSD: ventricular septal defect.

6. EXTRACORPOREAL LIFE SUPPORT FUNDAMENTALS AND DETAILS

6.1 Background

In its most elementary form, ECLS utilizes a pump to pull blood from the venous circulation, push it through a gas exchange device and then return the blood, now oxygenated and pressurized, to the patient's arterial tree. Historically, roller pumps were the most commonly used pumping devices for ECLS. There has been a gradual and sustained increase in the use of centrifugal pumps in ECLS circuitry during the past decade. Currently, centrifugal pumps are used in 100% of adult ECLS cases.

6.2 Centrifugal pumps

Centrifugal pumps use a spinning rotor to generate centrifugal force within a rigid housing to generate negative downstream (inlet) pressure and positive upstream (outlet) pressure. The rate of flow depends on blood volume within the housing, rotational speed of the pump and upstream resistance to flow (pressure). In contrast to roller pumps, centrifugal pumps may be positioned at or above the level of the patient. Centrifugal pumps are capable of generating flow rates >9 l/min. Modern centrifugal ECLS pumps use either a low friction axial pivot point or magnetic levitation to support the rotor within the housing for the pump head. Rotational force is achieved by coupling magnetic elements of the rotor within the pump head to an external rotating magnet. Centrifugal pumps are kinetically inefficient at extremely low and high flow (revolution) rates, which may lead to increases in shear stress and haemolysis. Despite these drawbacks, centrifugal pumps cannot create dangerous outflow pressures, and are less traumatic to blood.

6.3 Oxygenators

Soluble gas is removed from a patient's blood [carbon dioxide (CO_2)] or added to a patient's blood (O_2) within the ECLS circuit gas exchange device (oxygenator). Historically, blood flow through the gas exchange device was spatially separated from gas flow by a semipermeable membrane. Early silicone rubber membrane oxygenators were large and had comparatively high resistance to blood flow. Contemporary oxygenators utilize microporous hollow fibres to transfer gas through the blood path, which significantly increases efficiency of gas exchange while presenting reduced resistance to blood flow. Although several biomaterials have been used to create the gas exchange fibres, polymethylpentene hollow fibres are currently the ones most commonly used in ECLS gas exchange devices [36].

6.4 Circuitry integration

The typical ECLS circuit configuration includes drainage (inlet) tubing, a blood pump, an oxygenator and tubing (outlet) to return blood to the patient. Individual circuitry components may be combined or exchanged, depending on unique clinical needs,

REPORT

Downloaded from https://academic.oup.com/ejcts/article/59/1/12/5918808 by guest on 08 February 2021

Table 4: Principles to consider when choosing non-conventional post-cardiotomy ECLS system modes and configurations

Underlying disease (preoperative or intraoperative) (ischaemic/inadequate myocardial protection, valve disease with mechanical prosthesis, associated lung dysfunction or oedema)
Preoperative uni- or biventricular function (isolated RV versus isolated LV or biventricular dysfunction)
Adequacy of ECLS venous return
Adequacy of ECLS output (septic state) (if higher flow is required)
State of global cardiac contractility (very poor or absent contractility with high risk of intracardiac thrombosis)
Extent of left chamber stasis and distension
Adequacy and efficacy of aortic valve opening under ECLS support
Pulmonary insufficiency/congestion
Adequacy of upper body and/or coronary oxygenation
Presence and extent of peripheral arterial atherosclerosis
Presence of limb ischaemia (peripheral cannulation)
Presence of limb hyperperfusion (axillary artery perfusion with 'chimney technique')
Likelihood of ECLS weaning (bridge to VAD or HTx) (a prophylactic 'VAD-like' configuration for a prolonged temporary assistance with short-term mechanical assistance without oxygenator)
Possibility of patient mobility on ECLS (if prolonged support expected)

ECLS: extracorporeal life support; HTx: heart transplant; LV: left ventricle; RV: right ventricle; VAD: ventricular assist device.

patient characteristics and equipment availability. ECLS circuits typically incorporate 1 or more access points, which enable blood sampling and pressure transduction within the blood path. ECLS circuits that utilize a separate blood pump, oxygenator and monitoring equipment offer increased circuitry configuration flexibility and enable the exchange of a single component of the circuit if failure occurs. Many contemporary ECLS circuits utilize an integrated pump-oxygenator and internal monitoring circuitry. These integrated ECLS systems are generally smaller and more portable than non-integrated circuits, allowing a 'turnkey' solution to their application. Although they are ideally suited for implementation in the field and subsequent patient transport, it is at the expense of a non-integrated ECLS circuit in which failed components require the entire circuit to be replaced. Integrated circuits have advantages, as mentioned above, but they are significantly more expensive and, by design, are less malleable than non-integrated systems.

6.5 Extracorporeal life support flow

The goal of ECLS support is to provide adequate end-organ oxygen delivery. Consequentially, the ECLS pump flow rate is adjusted to meet a patient's unmet perfusion and oxygen delivery needs. When used to support PC patients experiencing LCO and respiratory insufficiency, initial ECLS flow rates may be set to achieve a full cardiac output (CO) equivalent or more, depending on the patient's changing perioperative metabolic demands. V-A ECLS flow may initially be set at 4.5–5 l/min or higher according to the metabolic needs but are subsequently reduced as oxygen debt has been paid back and native CO has increased as a result of myocardial recovery. Increased ECLS flow rates may be necessary to adequately support patients who experience septic shock or systemic inflammatory response syndrome. Adequacy of circulatory support with V-A ECLS support should be monitored using all of the same parameters of adequate end-organ oxygen delivery that one normally uses, i.e. blood pressure, urine output, serum lactate levels and mixed venous oxygen saturation. The set-up of ECLS flow should take into consideration the preceding factors, but also the potential shortcomings. Indeed, deleterious effects of high flow, such as haemolysis and thrombocytopaenia due to blood element destruction, as well as increasing LV afterload should lead to the consideration of unloading (discussed in Sections 6, 8, 9 and 11).

6.6 Gas management

Contemporary ECLS systems are highly efficient at gas exchange and capable of delivering fully oxygenated blood to a patient at even extremely high pump flow rates. Gas supplied to the ECLS gas exchange device may be 100% oxygen or blended oxygen/air. At progressively higher pump flow rates, increasing oxygen concentration may be required. Removal of CO_2 from circulating blood is accomplished by gas flow through the gas exchange device. Rate of CO_2 removal is proportional to the gas flow rate (sweep) through the exchange device (analogous to 'minute ventilation' on the ventilator). The gas flow rate is adjusted based on the patient's metabolic needs and CO_2 production. Adequacy of ECLS pump flow, gas flow rate and gas mixture ratio must be carefully and continuously monitored because frequent adjustments are often required to meet the changing needs of the patient.

6.7 Description of evidence

No RCTs have been performed to determine the superiority of specific circuitry components in the setting of PC-ECLS for adult patients. Current systems consistently use centrifugal pumps and polymethylpentene-fibre oxygenators. Developers continue to make ECLS systems more compact, miniaturized and portable, with haemodynamic, pump performance and blood-related data displayed [37]. Heparin-bonded circuits and cannulae [38], the appearance of polymethylpentene-based oxygenator fibres, and the move to centrifugal pumps for ECLS, represent the major technological advancements. The search for a more biocompatible circuit is under way, of particular importance in PC patients due to the inevitable higher extent of systemic inflammatory reaction secondary to the use of CPB. RCTs have not been performed to determine the superiority of a single class of ECLS gas exchange devices or the use of integrated pump-oxygenator circuitry over non-integrated ECLS circuits which allow for replaceable, individual components.

Although no specific document identifies the type of circuit best suited for a specific clinical scenario, the need to facilitate

Downloaded from https://academic.oup.com/ejcts/article/59/1/12/5918808 by guest on 08 February 2021

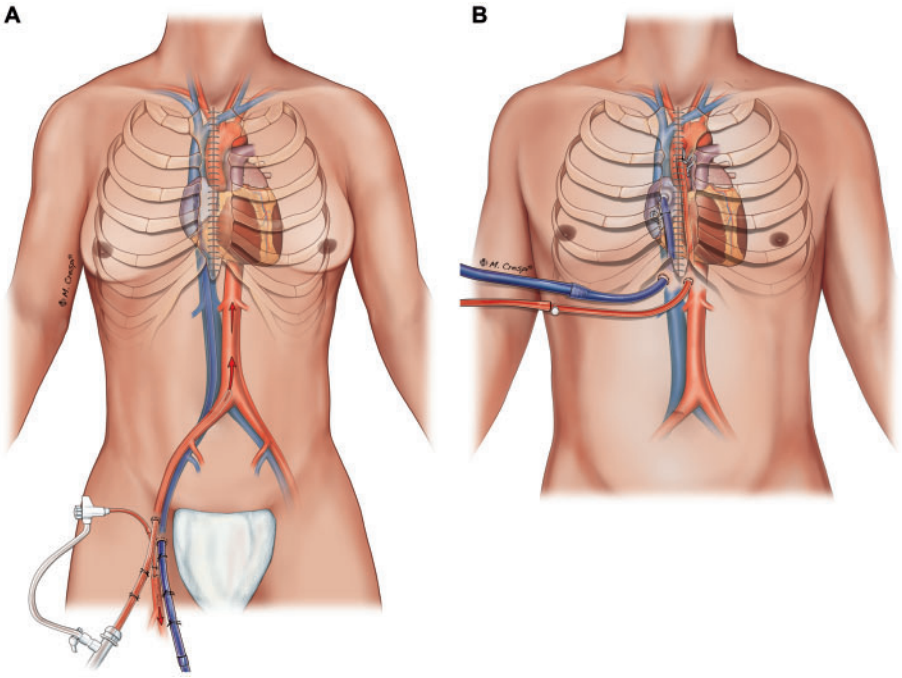

Figure 2: Several configurations of veno-arterial extracorporeal membrane oxygenation in post-cardiotomy patients. (**A**) Peripheral (femoral vessel) approach with distal perfusion cannula and (**B**) subxipoid cannula tunnelling with central approach.

Recommendations for specific circuitry components in the PC-ECLS system

Recommendations	Class[a]	Level[b]
Centrifugal ECLS pumps are recommended for adult patients with PC-ECLS.	I	C
Integrated, portable pump-oxygenator ECLS circuits may be considered (particularly for transport) for adult patients with PC-ECLS.	IIb	C

[a]Class of recommendation.
[b]Level of evidence.
PC-ECLS: post-cardiotomy extracorporeal life support.

patient transport (e.g. to another centre for continued management) (see Section 16) argues for a compact, portable device [39].

7. EXTRACORPOREAL LIFE SUPPORT MODE AND CONFIGURATIONS

7.1 Background

ECLS modes and configurations have recently changed remarkably. Conventional V-A ECLS requires cannulation of a vein to drain the patient's venous blood and of an artery for oxygenated, pressurized blood reinfusion. This emphasis may change, however, because drainage and reinfusion locations in the circulation can and should vary according to the haemodynamic and metabolic conditions of the patient which often change during the ECLS run. These concepts have led to new nomenclature for ECLS, now called 'hybrid ECLS', indicating more complex and dynamic approaches, including the use of additional cannulas or devices, rather than the 'one size fits all' approach used in the past [7, 40].

The optimal cannulation strategy and configuration mode for V-A ECLS during PCS, in terms of supporting myocardial recovery, patient management and avoiding complications, still remains to be determined [41]. There are no well-designed, prospective studies or relevant RCTs upon which to rely.

Which cannulas to place into which arterial or venous vessels for the initiation of ECLS support is usually a straightforward decision-making process. However, hypoxaemia, end-organ damage, inadequate ECLS flows, pulmonary and left atrial or LV blood stasis, LV dilatation and myocardial or limb ischaemia must be taken into consideration to avoid preventable complications (Table 4) [40].

The need to convert to a different ECLS modality frequently is not an error in planning but rather a necessary response to a change in the patient's and ECLS performance-related conditions [40, 42].

7.2 Evidence review

In PC-ECLS, a central configuration can be easily instituted utilizing the cannulas already in place for CPB. However, the benefit of central versus peripheral cannulation is controversial [41]. Both approaches carry advantages and disadvantages [31, 41–43]: central cannulation directs antegrade flow into the aorta and, given the use of a larger right atrial cannula, achieves better cardiac unloading. Furthermore, it avoids differential oxygenation (also named as North-South or Harlequin syndrome) between the lower and upper parts of the body. The peripheral technique allows sternal closure which may be beneficial in terms of bleeding and infectious complications. Axillary or subclavian cannulation for ECLS inflow has also been reported [42]. RCTs addressing optimal cannulation strategies and configurations in

Downloaded from https://academic.oup.com/ejcts/article/59/1/12/5918808 by guest on 08 February 2021

PC patients treated with ECLS do not exist (the technical details of cannulation are reported in Section 9). In the largest retrospective single-centre series available [31], no survival advantage with the use of central versus peripheral cannulation (Fig. 2) in 517 patients who required V-A ECLS after cardiac surgery is reported. Saeed *et al.* [43] compared the immediate changes in haemodynamics, arterial blood gas values and end-organ function of patients on either peripheral ECLS or central ECLS support, with no particular advantage noted in one cannulation technique over the other. Similarly, Kanji *et al.* [44] showed no differences in peripheral and central cannulations regarding the mean peak lactate level as a marker for end-organ and limb perfusion. In-hospital outcomes in patients with central or peripheral cannulation for PCS were reported in a recent meta-analysis [41] that included 1691 patients from 17 retrospective observational studies. There was no difference between the 2 techniques regarding all-cause mortality, nor between peripheral and central V-A ECLS with regards to cerebrovascular events, limb complications or sepsis rates. However, peripheral cannulation was associated with a significant reduction in the risk of bleeding, the transfusion of packed red blood cells, fresh frozen plasma and platelets, and, interestingly, the need for continuous veno-venous (V-V) haemofiltration. Besides, the meta-analysis did not show an increase in limb complications using a peripheral approach. Most recently, though, was a report of improved outcomes with peripheral cannulation over central access in a PCS population derived from a meta-analysis that showed lower in-hospital/30-day mortality [45].

The features and aspects related to cannulation are discussed in Section 9.

Recommendations for an oxygenator in the RV assist device circuit of the ECLS system (Oxy-RVAD)

Recommendations	Class[a]	Level[b]
The use of an Oxy-RVAD may be considered in patients with isolated preoperative or postoperative RV dysfunction and concomitant respiratory compromise.	IIb	C
The use of an Oxy-RVAD may be considered in patients with preoperative lung compromise at high risk for postoperative V-V ECLS or who need other forms of respiratory support.	IIb	C
The use of an Oxy-RVAD in patients undergoing acute pulmonary artery embolectomy with preoperative, intraoperative or postoperative RV failure occurrence is recommended.	I	C
The use of an Oxy-RVAD in patients undergoing pulmonary artery endarterectomy with preoperative, intraoperative or postoperative RV failure occurrence may be considered.	IIb	C

[a]Class of recommendation.
[b]Level of evidence.
Oxy-RVAD: external right ventricular-ventricular support with an oxygenator; RV: right ventricular; V-V ECLS: veno-venous extracorporeal life support.

7.3 Extracorporeal life support for isolated right ventricular failure

The presence of severe RV dysfunction in surgical patients, pre-existing or occurring intraoperatively or postoperatively, frequently presents a potentially lethal dilemma for the surgeon. PC RV dysfunction, at times associated with severe respiratory insufficiency, accounts for the majority of PC-ECLS indications. In these situations, a V-A mode is usually used, but the LV may not be compromised if the problem is isolated RV failure. In contrast to what had been a lethal complication, temporary support is now capable of addressing isolated RV chamber impairment, with or without the addition of gas exchange support for the lung. The configuration of isolated right heart support associated with an oxygenator in the RVAD circuit, named 'Oxy-RVAD', describes the combination of isolated RV support with extracorporeal gas exchange.

This configuration in PC-ECLS may provide several advantages over V-A ECLS. Indeed, the oxygenator may be removed once lung function is recovered, while maintaining RV assistance, should extended RV support be necessary. In this situation, removal of the oxygenator may decrease dependence on therapeutic anticoagulation as well as avoid oxygenator-related complications, such as haemolysis and clot formation.

The Oxy-RVAD configuration, moreover, may also be used as pure V-V ECLS in the case of RV recovery, but with the persistence of lung dysfunction. Indeed, such an ECLS mode may provide the advantage of no concern about the potential occurrence of RV failure secondary to increased pulmonary artery (PA) pressure during V-V ECLS, which is observed in up to 20–25% of patients with acute respiratory distress syndrome (ARDS). This configuration enhances V-V ECLS efficacy by avoiding virtually any recirculation as ECLS inflow derives from the right atrium with outflow to the PA.

Oxy-RVAD may be achieved with double or single cannulation, depending on the cannula used, and is also amenable to a fully percutaneous approach.

7.4 Hybrid extracorporeal life support configurations

Conversion from V-V to V-A or from V-A to V-V or more complex modes may be advisable based on changing clinical conditions. In the international summary report of ELSO, hybrid ECLS represents ~2% of all documented ECLS runs [40]. Patients on V-V ECLS can have haemodynamic deterioration (secondary to RV, LV or biventricular failure) and can require cardiocirculatory support [7, 40]. This support can be achieved by the addition of an arterial perfusion cannula to the circuit and inverting the flow from the perfusion cannula in the venous side, realizing, therefore, a double-draining system from the right side (V-V-arterial ECLS), and which can provide circulatory support via the femoral or subclavian artery [40, 46–48]. In situations where V-A ECLS does not provide sufficient oxygenated blood to the upper body of the patient, an extra inflow cannula can be introduced into the internal jugular vein, and oxygenated blood can be delivered to the right atrium and thus to the pulmonary circulation, i.e. the V-VA ECLS approach [7, 40]. The addition of oxygenated blood returning to the right side of the heart can effectively correct differential aortic hypoxaemia by providing oxygenated blood through the pulmonary circulation to the left side and thus to the coronary arteries and aortic arch vessels. Werner *et al.* [42] described the outcome of 23 adult and 8

Downloaded from https://academic.oup.com/ejcts/article/59/1/12/5918808 by guest on 08 February 2021

paediatric patients supported with V-VA ECLS. The reason for conversion to the V-VA ECLS configuration was cardiac failure (46%), differential oxygenation (38%) and worsening hypoxia (15%) in the adults, whereas in the paediatric group, the reasons were cardiac failure (29%), differential oxygenation (42%) and worsening hypoxia (29%) [42]. Survival rates were 39% in adults and 71% in paediatric patients, with neurological complications occurring in 13% of the adult cases and 29% of the paediatric patients, respectively. In the hybrid ECMO series (21 adult patients) reported by Biscotti *et al.* [48], the survival to hospital discharge was 43%. Conversion from initial V-V to V-VA was required in 8 patients, whereas from V-A to V-VA was required in 2. Indications for conversion from V-V ECLS to V-VA ECLS included RV failure, cardiogenic shock or progressive non-septic shock. Indications for conversion from V-A ECLS to V-VA ECLS included differential upper and lower body oxygenation with hypoxic coronary and cerebral flow. The comparison of different ECLS configurations reported by Stohr *et al.* [49] in 30 patients affected by severe ARDS showed greater survival advantage in the V-VA group (73%) compared to the V-A (25%) and V-V (37%) groups. The application of an additional cannula during ECLS support, either to the left or right side (Supplementary Material, Table S4), however, should be considered with caution due to the increased risk of bleeding, particularly when accessing the arterial vasculature [50]. Furthermore, besides the vascular complications, the presence of a third or fourth cannula theoretically represents another site for infection or thrombosis.

Additional ECLS configurations, besides conventional V-V or V-A, are therefore possible, represent a valuable tool in enhanced ECLS patient management, and account for the drainage capacity, reinfusion need, haemodynamic status and cannula type utilized (single-lumen, double-lumen), including the possibility to change the flow direction in the same cannula, as above-mentioned [7, 40, 48].

Recommendations for ECLS modes and configurations

Recommendations	Class[a]	Level[b]
Peripheral cannulation approach should be considered in patients with PCS and for V-A ECLS in the presence of LV or biventricular failure [41, 43–45].	IIa	B
Oxy-RVAD configuration may be considered in the presence of PC refractory isolated RV failure.	IIb	C
In the presence of limb ischaemia despite antegrade perfusion, contralateral femoral artery, axillary artery or central access should be considered.	IIa	C
Axillary/subclavian artery or central aortic cannulation for patient inflow may be considered as an alternative to femoral artery cannulation.	IIb	C
Direct cannulation of the LV through the apex may be considered for LV drainage and for conversion to an LVAD-like configuration (LV apex-subclavian artery).	IIb	C
Alternative, hybrid, ECLS configurations (VV-A, V-VA or other configurations, including additional devices) may be considered in patients on V-V ECLS or V-A ECLS with cardiac failure, differential oxygenation (also known as Harlequin syndrome), respiratory failure, refractory hypoxaemia, insufficient venous drainage and/or LV stasis.	IIb	C
In the presence of infrequent haemodynamic or structural cardiac conditions, the use of associated devices (ECLS + IABP or transseptal or transaortic suction device) should be considered.	IIa	C

[a]Class of recommendation.
[b]Level of evidence.
ECLS: extracorporeal life support; IABP: intra-aortic balloon pump; LV: left ventricular; LVAD: left ventricular assist device; oxy-RVAD: oxygenator in right ventricular assist device circuit; PC: post-cardiotomy; PCS: post-cardiotomy shock; RV: right ventricle; VV: veno-venous; VV-A: veno-venous-arterial; V-VA: veno-venousarterial.

7.5 Combinations of devices

In the presence of several haemodynamic or structural cardiac conditions, a combination of devices (ECLS + an additional temporary MCS system or cannula) might be necessary to enhance circulatory support or overcome several shortcomings or complications, such as LV stasis, differential oxygenation or other cardiac conditions (e.g. mechanical valve prostheses) (Supplementary Material, Table S4). Further discussion is found elsewhere in Sections 7 and 8. Besides the historical combination of ECLS and intra-aortic balloon counterpulsation (IABP), a recent increase in the experience of ECLS and Impella (Abiomed Inc., Danvers, MA, USA), the so-called 'ECMELLA', has been described and is discussed in 'Left heart venting' in Section 9.

8. INTRA-AORTIC BALLOON PUMP AND CONCOMITANT CARDIOCIRCULATORY ASSISTANCE ALTERNATIVES

8.1 Introduction

Although V-A ECLS is increasingly the primary mode of PC support, there are alternatives that merit consideration. In many cases, short-term univentricular support devices are used before initiation of ECLS. Whereas true RCTs are lacking, there is evidence for the efficacy of treatment algorithms that incorporate alternate forms of temporary cardiocirculatory assistance.

8.2 Intra-aortic balloon pump and alternate short-term mechanical circulatory support platforms

The IABP remains the mainstay for and first approach to PCS management. Its safety profile, ease of insertion and efficacy in many patients, particularly those with underlying coronary ischaemic disease, makes its use appropriate and reasonable. Prognostication after an IABP implant in patients with PCS has been described and may be useful in characterizing patients at higher risk for subsequent further deterioration calling for more aggressive circulatory support [35]. However, the benefit of the concomitant use of IABP with ECLS is unclear. In the reviewed

REPORT

Downloaded from https://academic.oup.com/ejcts/article/59/1/12/5918808 by guest on 08 February 2021

PC-ECLS series, the simultaneous application of ECLS with an IABP ranged from 12% to 100% [51]. Although some of the variability may be accounted for by the heterogeneity of each patient's disease process, it certainly highlights the lack of certainty regarding the benefits of ECLS with IABP support. When used concomitantly, the IABP enhances flow pulsatility while decreasing LV afterload, thus improving LV ejection [52] and reducing LV wall tension [53–56]. As a result, the IABP reduces intracardiac blood stasis theoretically by decreasing the risk of intracardiac clot formation.

In primary cardiogenic shock, the IABP has been the most widely used ST-MCS device for decades [57, 58]. After the neutral results of the IABP-SHOCK II trial [59, 60], European guidelines downgraded routine IABP use in cardiogenic shock to a class III B recommendation [61, 62]. These data compelled teams to use alternative ST-MCS platforms [3, 58]. Among the currently available platforms are percutaneous devices, the TandemHeart™ (TandemHeart, Cardiac Assist/LivaNova, Pittsburgh, PA, USA), and axial flow MCS from the Impella® family (Impella 2.5 and Impella CP, Abiomed Inc.), all of which are used for short-term support [3, 57, 63]. The Centrimag (Abbot, Inc. Minneapolis, MN, USA) system is used in an open surgical platform for both short- and intermediate-term support.

8.3 Evidence review

8.3.1 Intra-aortic balloon pump. RCTs focusing on the use of alternative or concomitant ST-MCS devices in PC patients do not exist. Moreover, there are no large meta-analyses dealing with this topic in surgical patients. However, a meta-analysis [57] including 4 randomized trials (including 158 patients) compared the use of TandemHeart or Impella to IABP in patients with cardiogenic shock. There was no difference in 30-day mortality for active MCS compared with IABP. MCS significantly increased mean arterial pressure and decreased lactate levels at comparable cardiac index and pulmonary capillary wedge pressure. No significant difference was observed in the incidence of leg ischaemia, whereas the rate of bleeding was significantly increased in MCS compared to IABP [57].

It is a reasonable conclusion that the IABP in the setting of PC-ECLS may have limited universal benefit [64, 65]; there are reports of both improved survival [31, 66] and no difference in survival [32, 67–69].

The utility of IABP in cardiac surgery was recently analysed, and recommendations about its use in patients who experience difficult weaning from CPB or even in patients with preoperative or at high-risk for perioperative cardiac decompensation, are clearly provided [70]. Furthermore, the advantage of concurrent compared to delayed implantation of IABP with ECLS for PCS has also been recently shown, making such an immediate combination a potentially favourable decision-making tool compared to a delayed IABP implant after initiation of ECLS [71]. For the time being, the use of IABP in the presence of LV or biventricular PCS may be considered. In cases of an intraoperative ECLS implant, a concurrent application should be considered, although additional studies are warranted to conclusively provide evidence in this regard.

8.3.2 Impella. Catheter-based flow pumps provide univentricular support and may be implanted either centrally or peripherally, either percutaneously/peripherally or via direct surgical implantation. Engstrom *et al.* [72] reported a total of 46 patients with PCS in 3 European centres who were treated with the Impella 5.0 (Abiomed Inc.). Most of the patients underwent CABG (48%) or combined surgery (33%); half received an IABP prior to the Impella 5.0-implant; the estimate of overall 30-day survival was 39.5% [72]. Griffith *et al.* [73] described 16 PC patients similarly treated with the Impella 5.0 [73] who had immediate haemodynamic improvement. Recovery of the native heart function sufficient to support the circulation occurred in 15 of 16 patients, with 1 patient bridged to another therapy. Survival at 30 days, 3 months and 1 year was 94%, 81% and 75%, respectively. Use of the largest Impella (Impella 5.0) as an isolated ST-MCS for LV dysfunction in patients with PCS is limited, but the only single-centre study reported favourable results [74]. A more recent modification of this device has been designed (Impella 5.5 device, Abiomed Inc.), but no outcomes in the setting of PCS are available.

A right-sided device, the Impella RP (Abiomed Inc.), may also be used in PCS, but, again, no large series of patients exists to allow determination of its effectiveness for PC RV failure.

8.3.3 TandemHeart. In a randomized trial comparing cardiogenic shock patients treated with IABP versus the percutaneous TandemHeart (TandemHeart, Cardiac Assist/LivaNova), haemodynamic and metabolic parameters were reversed more effectively by this ST-MCS than by standard treatment with the IABP. However, more complications were encountered when using the invasive TandemHeart procedure [75]. This platform may be used in the PCS setting but remains a univentricular platform. It may be reconfigured to support the RV but the device was not designed for this purpose.

8.3.4 Short-term ventricular assist devices. A variety of durable and intermediate ventricular assist device platforms have been used in PCS. The available literature on short-term VADs comprises only a few older studies. Hernandez *et al.* in 2007 [76] reported an overall survival rate to discharge after VAD placement in PC patients of 54.1%. In 2009 the results of Xiao *et al.* [77] were comparable with a 41.2% PC patient survival. More recently, the Centrimag platform has been configured to provide intermediate support. Ando *et al.* [78] reviewed more than 250 patients from Columbia Presbyterian Hospital. Although the report included many patients with primary cardiogenic shock, the study demonstrated improvements in overall survival to discharge from 43% to 57% over the decade.

The application of IABP or transvalvular microaxial pumps may be considered, in association with ECLS, to favour LV unloading in case of a poor or absent aortic valve opening at the initiation of ECLS at the chosen maximal flow as discussed in Sections 6 and 9.

Downloaded from https://academic.oup.com/ejcts/article/59/1/12/5918808 by guest on 08 February 2021

Recommendations for IABP and alternative ECLS platforms

Recommendations	Class[a]	Level[b]
The implantation of an IABP may be considered timely in cases of ventricular dysfunction of intermediate severity during weaning from CPB prior to initiating ECLS.	IIb	C
The implantation of an IABP may be considered timely in the presence of acute heart failure shortly after weaning from CPB prior to initiating ECLS.	IIb	C
Implantation of an IABP may be considered in association with an ECLS implant in the presence of poor or absent aortic valve opening at the start of ECLS with the chosen flow.	IIb	C
The implantation of an IABP is not recommended in cases of severe LV or biventricular dysfunction as a primary treatment option in case of impossible CPB weaning or acute heart failure shortly after CPB weaning.	III	C
The application of a percutaneous or axillary artery transvalvular microaxial device (Impella 5.0) in PC patients may be considered a primary or concomitant treatment option with ECLS in the presence of severe isolated LV dysfunction.	IIb	C
The application of a percutaneous or transaortic or transaxillary transvalvular microaxial device in PCS may be considered in the presence of a poor or absent aortic valve opening at the start of ECLS with the chosen flow.	IIb	C
The application of short-term VADs in PC patients (isolated RV dysfunction) may be considered a primary treatment option.	IIb	C

[a]Class of recommendation.
[b]Level of evidence.
CPB: cardiopulmonary bypass; ECLS: extracorporeal life support; IABP: intra-aortic balloon pump; LV: left ventricular; PC: post-cardiotomy; PCS: post-cardiotomy shock; RV: right ventricular; VAD: ventricular assist device.

9. IMPLANT

9.1 Background

Considerations in ECLS implantation in PC patients involve the timing and location of the implant, the configuration strategy, the need for LV unloading and the predictability of recovery or need of a prolonged support. Unfortunately, there are no relevant RCTs or large meta-analyses to guide any decision-making on this topic.

9.2 Evidence review

9.2.1 Timing and location. The timing of ECLS implantation after surgery is obviously dictated by the patient's and the underlying cardiac conditions, e.g. intractable pump failure with inability to safely separate from CPB or shortly after or during the postoperative ICU phase. In the largest retrospective single-centre clinical study, which included more than 500 patients with PCS, ECLS was established during the initial cardiac surgery intraoperatively in almost 42% of the cases [31]. In this study, the mean interval from the primary cardiac procedure to initiation of ECLS in these patients was 62.6 h, with less delay associated with improved survival, although postoperative ECLS implant was not associated with a higher in-hospital mortality compared to intraoperative ECLS implantation [31]. However, in a recent meta-analysis, the majority of reported series have shown a greater frequency of intraoperative implants compared to the ICU setting [79], as was confirmed in other series [2, 80, 81]. Delayed identification of the LCO syndrome and the clinical status of the patient may also play a role in the timing of the implant [16]. The higher incidence of unfavourable outcomes in the presence of advanced poor end-organ perfusion at the time of ECLS implant [34, 80] indicates that the early implant of ECLS is highly recommended, most likely in the operating room, if signs of refractory acute cardiac failure develop despite adequate pharmacological and partial mechanical assistance (IABP) as well as after sufficient time (reperfusion) for myocardial recovery according to the type and duration of ischaemic time.

A delay in placing the ECLS, particularly in the presence of RV dysfunction, has been linked to a high incidence of unfavourable outcomes [31, 82], suggesting that an aggressive approach should be implemented in such a setting because the RV is more vulnerable in the perioperative phase and is less responsive to pharmacological or other conservative management.

9.2.2 Cannulation. In-hospital outcomes in patients with central or peripheral cannulation for PCS have been reported in recent meta-analyses [41, 45] and are addressed in Section 7. The peripheral approach is more commonly adopted [41, 45] and, in some series, is the only access used [34, 54]. In the meta-analysis of Biancari *et al.* [79] (23 studies including 2652 patients), the primary arterial cannulation strategy was peripheral in 79.0% of the patients. Central cannulation was the unique access in only 1 series [52]. In the case of peripheral cannulation, open as opposed to percutaneous cannula placement was chosen in the majority of the series [49, 68, 83, 84] and was associated with fewer complications than the percutaneous approach [52, 68, 83, 84]. Rastan *et al.* [31] showed that femoral venous drainage was associated with worse prognosis, suggesting that suboptimal right-sided decompression had a negative impact on ECLS flow and management. Alternative approaches, e.g. arterial inflow via the subclavian artery with either peripheral [84–86] or central [86] cannulation for venous return, have been reported. In larger series of patients [31, 80, 87], axillary arterial cannulation was adopted in ∼12% of the cases. Compared to aortic and femoral artery cannulation, axillary access is more frequently used in the operating room and has a significantly higher rate of vascular complications (particularly fasciotomy and amputation) and bleeding at the cannulation site [87]. The use of a right anterior minithoracotomy for ascending aorta, RA and pulmonary vein (for venting) access, has also been described [87, 88].

Small femoral arterial cannula size, distal perfusion cannulas and the use of a vascular graft anastomosed end-to-side to the femoral artery are commonly advocated [12, 31, 44, 45, 89, 90] to avoid ischaemia-related complications of the cannulated limb. In a meta-analysis including 22 retrospective

REPORT

Downloaded from https://academic.oup.com/ejcts/article/59/1/12/5918808 by guest on 08 February 2021

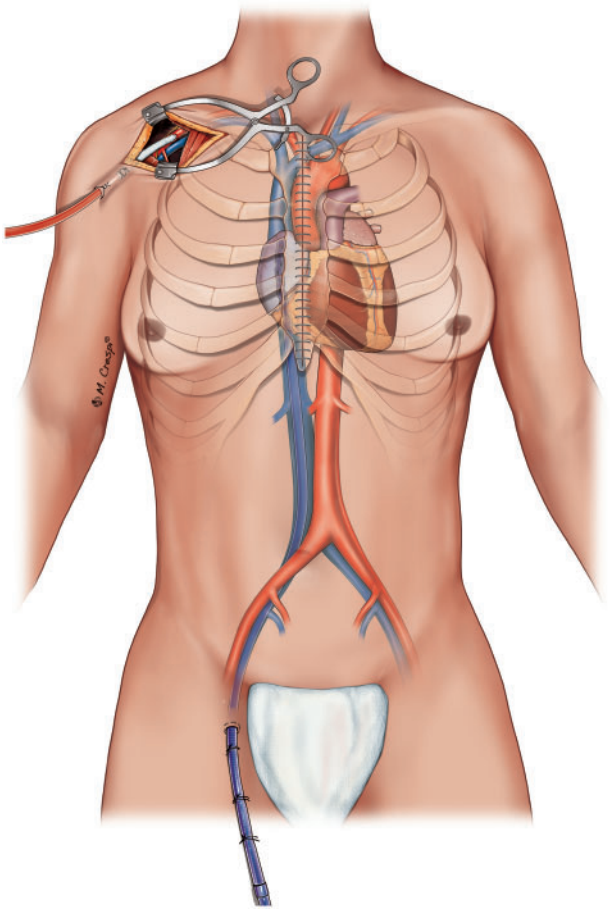

Figure 3: Peripheral veno-arterial extracorporeal membrane oxygenation with axillary artery ('chimney technique' with graft interposition) as the perfusion port.

observational studies, the presence of a distal perfusion cannula was associated with at least a 15.7% absolute reduction in the incidence of limb ischaemia despite the fact that there was a significant variation in cannula indication, cannula type and cannula placement techniques among the studies [45]. With the peripheral approach, open cannulation appears to be associated with fewer complications than full percutaneous access [68, 83]. Finally, continuous monitoring of the adequacy of limb perfusion is no different from the management applied in other ECLS settings with peripheral arterial access utilizing infrared spectrometric assessment of HbO_2 saturation [40, 91] as discussed in Sections 10 and 12.

Axillary or subclavian artery cannulation (Fig. 3) in cases of severely arteriosclerotic or small femoral arteries, which theoretically should allow a 'pseudocentral' flow compared to femoral artery or ascending aorta cannulation, has been recently investigated [87, 92]. However, compared to aortic and femoral arterial cannulation, a recent study assessing this technique reported more vascular access complications, bleeding and cerebrovascular accidents [93]. In a large series of subclavian V-A ECLS using the side graft cannulation technique, hyperperfusion of the ipsilateral arm was the most common complication, occurring in 25% of patients [94]. Moreover, bleeding from the cannulation site requiring surgical re-exploration appears more frequently after subclavian artery cannulation than after femoral or central cannulation [94].

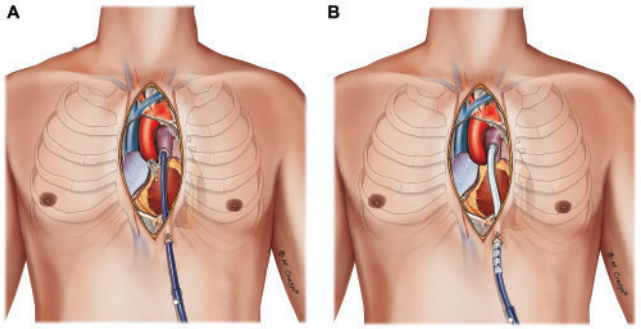

Figure 4: (**A**) Direct pulmonary artery cannulation. (**B**) Pulmonary artery cannulation through a prosthetic graft.

Surgical or percutaneous cannulation of the PA (Figs 4 and 5) may provide additional ECLS possibilities and configurations, particularly for RV, biventricular or V-V ECLS support [95]. The major advantages of this cannulation technique include (i) in respiratory failure, limited or absent recirculation associated with immediate RV support; (ii) in RV failure, using the ECLS outflow arm to the PA as an RVAD totally bypassing the RV; or (iii) using the PA cannula to enhance right and left heart drainage with more efficient LV and RV unloading.

Recently, Napp *et al.* [96] reported a first-in-man case of a fully percutaneous cardiac assistance device using the right atrium/PA approach for RV bypass and a transaortic device for LV support.

As suggested previously, Avalli *et al.* [97] used a percutaneous PA catheter for ECLS inflow, thereby increasing LV unloading. Although it may not be as effective as direct LV unloading, PA cannulation provides significant additional drainage of the right heart, avoiding the need for left-sided cardiac access to unload the LV, e.g. right superior pulmonary vein cannulation, atrial septostomy or intraseptal or cardiac apex cannulation [98]. Furthermore, percutaneous PA cannulation in the perioperative setting, under fluoroscopic guidance, with femoral venous drainage, avoids the need for chest reopening at the time of ECLS decannulation. Percutaneous cannulation may be performed with a single- or double-lumen cannula (Fig. 5) [99].

Clearly, direct cannulation of the LV through its apex by means of a left minithoracotomy provides optimal LV drainage and unloading [100] but can also be used as inflow for ST-MCS (Fig. 4) [46]. A large apical cannula definitively treats LV distention, but when weaning from ECLS fails, it allows for conversion to an LVAD based on this cannula [46, 88]. Transthoracic echocardiography is recommended to localize the true apex of the LV and determine the correct interspace due to variability in its location resulting from differences in patient anatomy and degree of cardiac dilation [88].

9.2.3 Left heart venting. Whether a patient is centrally or peripherally cannulated, LV distension in the setting of severe ventricular dysfunction can be problematic due to increased afterload to the poorly contractile LV and could impact the prognosis for ventricular recovery. V-A ECLS usually results in effective right-sided cardiac drainage but may not be as effective in decompressing the left side. Furthermore, failure of the aortic valve to spontaneously and effectively open increases

Downloaded from https://academic.oup.com/ejcts/article/59/1/12/5918808 by guest on 08 February 2021

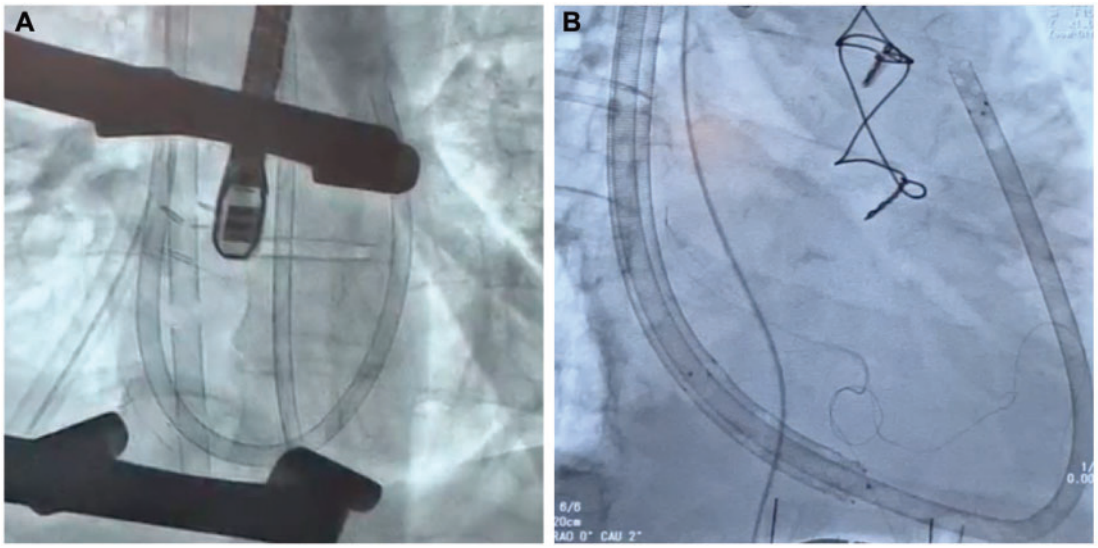

Figure 5: Post-cardiotomy percutaneous pulmonary artery cannulation with a single-lumen (**A**) (Medtronic Biomedicus Cannula, Medtronic Inc., Minneapolis, MN, USA) or dual-lumen (**B**) cannula (ProtekDuo, TandemLife, LivaNova, Pittsburgh, PA, USA) from the right internal jugular vein to support a postoperative failing right ventricle.

Method	Factor	Grade of severity			
Arterial line					
	Arterial Pulsatility	Mild weakness	Moderate weakness	Almost Pulseless	Less Invasive LV Unloading Manoeuvers To Be Applied
Central venous Line					
	$ScvO_2$	75-55%	55-45%	<45%	
	CVP	8-12 mmHg	12-16 mmHg	> 20 mmHg	
Echocardiogram					
	AV	Opening every 2 bpm	Opening every 3-4 bpm	Closure	IABP + Less Invasive LV Unloading Manoeuvers To Be Applied
	LV distension	Mild	Moderate	Severe	
	LA distension	Mild	Moderate	Severe	
	"Smoke like" effect	Mild	Moderate	Severe	
	IVC dilatation[1]	1.5 to 2.5 cm	>2.5 cm	>2.5 cm	
	IVC collapse[2]	<50%	<50%	No change	
Swan Ganz Catheter					
	PCWP	13-18 mmHg	18-25 mmHg	>25 mmHg	Invasive Catheter-Based LV Unloading Manoeuvers To Be Applied
Chest X-ray					
	Congestion[3]	Alveolar edema	Interstitial edema	Redistribution	

$ScvO_2$: central venous blood oxygen saturation; CVP: central venous pressure, AV: aortic valve; bpm: beats per minute; LV: left ventricle; LA: left atria, PCWP: post capillary wedge pressure.

Figure 6: Criteria to be used for the assessment of left ventricular unloading need (modified from Meani *et al.* [101]). AV: aortic valve; CVP: central venous pressure; IABP: intra-aortic balloon pump; IVC: inferior vena cava; LA: left atria; LV: left ventricle; PCWP: post-capillary wedge pressure; $ScvO_2$: central venous blood oxygen saturation.

the risk of blood stasis and thrombus formation, subendocardial ischaemia and progressive pulmonary congestion [55]. The actual prevalence of significant LV distension and stasis is unclear, ranging from 2% to 3% to more frequent rates. This aspect is receiving increasing attention, and more precise definitions and criteria are becoming more commonly utilized, provided that such a state is timely and appropriately assessed. Therefore, LV unloading-related aspects must be continuously monitored, as discussed in Section 12 (Fig. 6). In these circumstances and in the presence of initial signals of LV distension and stasis, non-aggressive strategies, including reduced ECLS flow, vasodilation, moderate inotropic drug dosages and adjusted ventilatory parameters to enhance RV drainage from the ECLS cannula, should be considered (Fig. 6). The use of IABP has been shown to effectively enhance LV unloading in the majority of cases with ineffective LV ejection [101]. The presence and extent of aortic valve opening are critical factors to be examined in relation to LV unloading [101] (Fig. 6). These aspects are clearly assessed by direct echocardiographic evaluation but are also indirectly evaluated by checking the pulse-pressure, that is the degree of blood pressure pulsatility. Pulsatility of <15 mmHg is considered at risk for subsequent LV stasis and distension [101]. IABP has been shown to be useful when no aortic valve opening or a lack of pulsatility is observed on ECLS, by enhancing LV ejection by reducing the afterload and enhancing the aortic valve opening [102]. If LV distension and stasis become critical, conservative approaches, including the IABP employment, may not be sufficient: more aggressive options may be, therefore, required, and catheter- or device-based interventions should

REPORT
Downloaded from https://academic.oup.com/ejcts/article/59/1/12/5918808 by guest on 08 February 2021

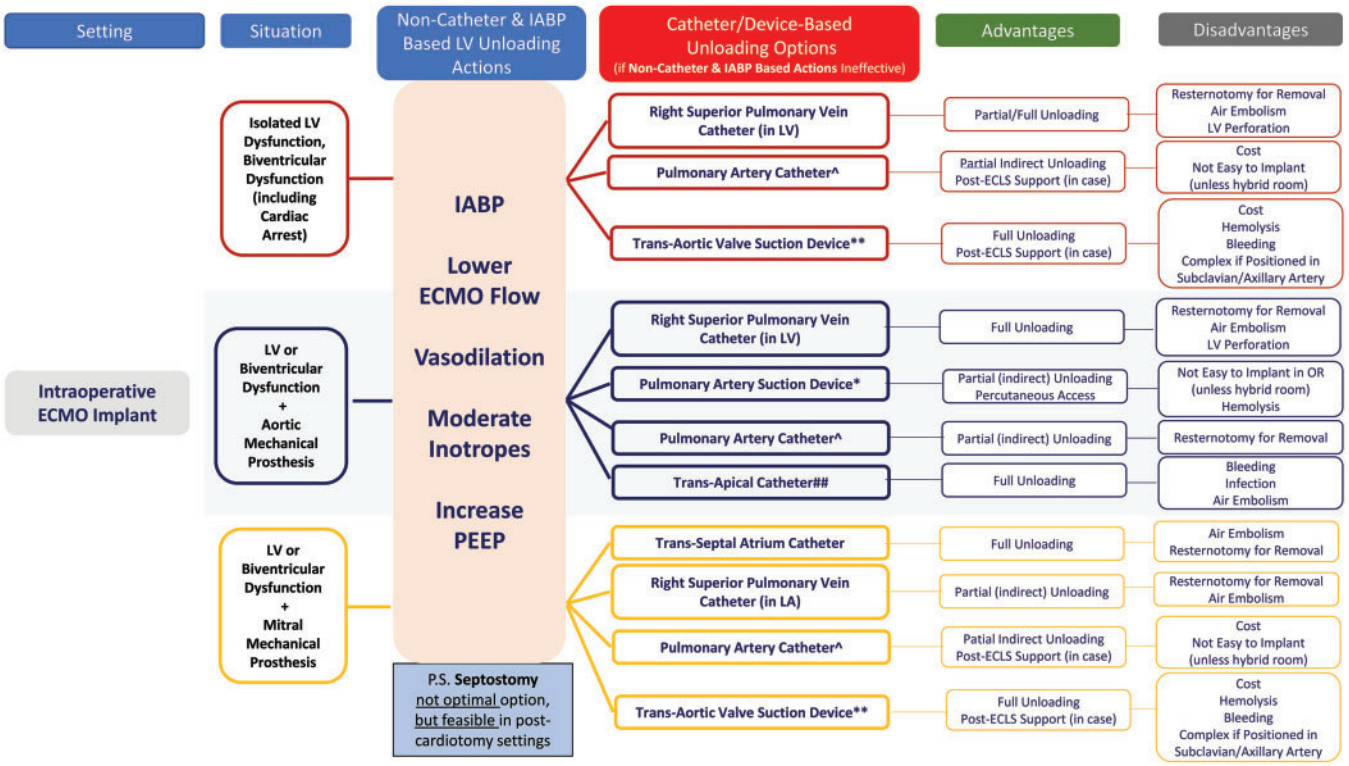

Figure 7: Procedures to enhance left ventricular unloading during veno-arterial ECMO in intraoperative post-cardiotomy shock. **Impella (Abiomed Inc., Danvers, MA, USA), *Impella RP (Abiomed Inc.), ^^single-lumen cannula; ##single- or double-lumen cannula. ECLS: extracorporeal life support; ECMO: extracorporeal membrane oxygenation; IABP: intra-aortic balloon pump; LV: left ventricle; PEEP: positive end expiratory pressure.

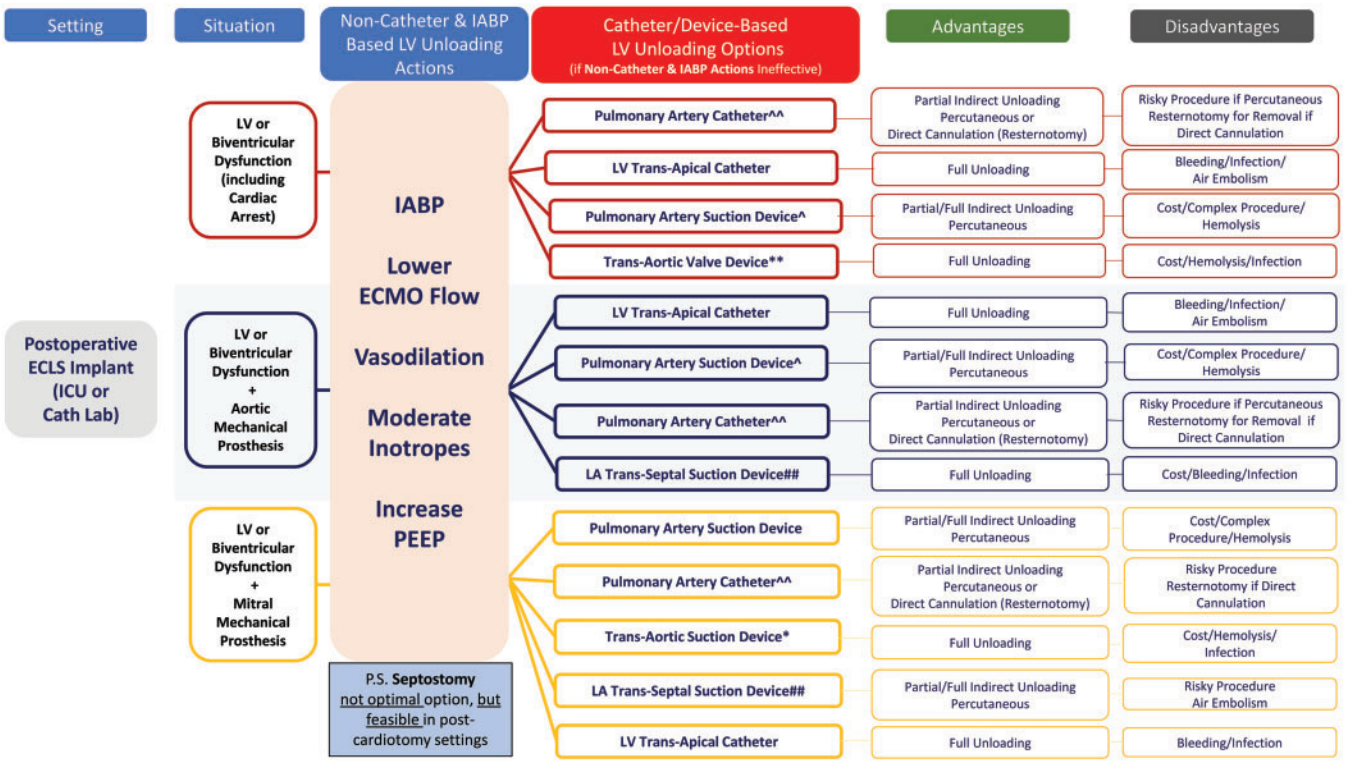

Figure 8: Procedures to enhance left ventricular unloading during veno-arterial ECMO in postoperative post-cardiotomy shock. **Impella (Abiomed Inc., Danvers, MA, USA); *Impella RP (Abiomed Inc.); ^^single- or double-lumen cannula. ECLS: extracorporeal life support; ECMO: extracorporeal membrane oxygenation; IABP: intra-aortic balloon pump; ICU: intensive care unit; PEEP: positive end expiratory pressure.

Downloaded from https://academic.oup.com/ejcts/article/59/1/12/5918808 by guest on 08 February 2021

be applied. Indeed, the addition of a left-sided catheter or device to directly unload the left cardiac chambers through the aortic valve (Impella, Abiomed Inc.), through the interatrial septum (TandemHeart, Cardiac Assist/LivaNova) or alternative accesses to indirectly unload via enhanced right-sided drainage or the IABP, is usually warranted when no or poor LV contractility is present, usually characterized by protracted aortic valve closure, and in the case of high ECLS flow required to guarantee end-organ perfusion. If no IABP or catheter-based left heart unloading is considered, the use of transvenous septostomy is also an option, although it is less easily controlled and should be performed only in centres with experience with the procedure. It is a rarely utilized option in PC-ECLS (Figs 7 and 8). A surgically placed catheter in the left atrium or ventricle or a similarly placed suction device may be the most dependable approach for LV decompression [103, 104]. When cannulating centrally, it is advisable to consider direct LV venting either through the right superior pulmonary vein, the aortic valve with a suction device (transfemoral or through the subclavian/axillary artery, or the ascending aorta) or the LV apex or by increasing indirect LV unloading with an additional vent in the PA (Fig. 9). In a recent review of both case series and retrospective studies in global ECLS experiences [55], the most common sites for LV decompression were the LA (31%), followed by indirect unloading via the IABP (27%), the transaortic route via an Impella (27%), direct apical LV access (11%) and the PA (4%). The percutaneous transseptal approach was reported in 22% of the total LV unloading procedures. The unloading was conducted surgically in 16%, roughly two-thirds via a median sternotomy and one-third via a minimally invasive procedure.

It is crucial to monitor vent lines to ensure adequate flow and avoid stasis and thrombosis. An inactive vent will serve as a nidus for thrombus formation. Real-time flow probe monitoring is advisable to avoid this complication.

How often LV venting is necessary, however, remains controversial. Because venting is an additional aggressive procedure (i.e. additional cannulation), expensive and not easily available (transaortic suction device), it may be underutilized. Use of this procedure varied widely, from no venting to 100% of patients undergoing a concomitant IABP implant [2]. The lack of evidence about the impact of LV venting on patient outcome, particularly in PC-ECLS, makes it impossible to provide conclusive recommendations for its use as a prophylactic procedure. It is also not possible to recommend a specific type of tool or technique, unless, as described, signs of LV distension and stasis occur predisposing to intracavitary thrombosis and lung oedema if left untreated.

Recommendations for implantation technique of ECLS system

Recommendations	Class[a]	Level[b]
Peripheral cannulation should be considered in patients with PCS [41, 45].	IIa	B
In peripheral ECLS with femoral artery cannulation, a distal perfusion cannula should be considered to reduce the risk of limb ischaemia [89].	IIa	B
Retrograde limb perfusion via the posterior tibial artery may be considered in the presence of limb ischaemia.	IIb	C
Small cannula size or insertion of a vascular graft in selective patients (peripheral vascular disease, small arterial size) may be considered in order to reduce the risk of limb ischaemia.	IIb	C
Open (pseudo percutaneous) compared to percutaneous cannulation may be considered in patients with peripheral PCS.	IIb	C
Ultrasound-guided vascular access should be considered if percutaneous cannulation is performed.	IIa	C
Axillary/subclavian artery cannulation for patient inflow may be considered as an alternative to femoral artery cannulation, particularly for prolonged support and patient mobility.	IIb	C
In the presence of signs of LV distension and stasis, protracted aortic valve closure and pulmonary oedema, it is recommended that conservative actions (non-catheter-based), including IABP, be instituted to enhance LV unloading [55, 101].	I	B
In the presence of signs of LV distension and stasis, protracted aortic valve closure and pulmonary oedema, septostomy may be considered.	IIb	C
In the presence of signs of LV distension and stasis, protracted aortic valve closure and pulmonary oedema that are unresponsive to conservative actions and an IABP, aggressive catheter-based or another device is recommended to enhance LV unloading [55, 101].	I	B
Direct cannulation of the LV through the apex may be considered for LV drainage and for conversion to an LVAD-like configuration (LV apex-subclavian artery).	IIb	C
Surgical or percutaneous cannulation of the PA may be considered for indirect LV unloading.	IIb	C

[a]Class of recommendation.
[b]Level of evidence.
ECLS: extracorporeal life support; IABP: intra-aortic balloon pump; LV: left ventricle; LVAD: left ventricular assist device; PA: pulmonary artery; PCS: post-cardiotomy shock.

10. MANAGEMENT OF INITIATION OF INTRAOPERATIVE EXTRACORPOREAL LIFE SUPPORT

As mentioned in Section 4.2, cardiogenic shock following cardiac surgery with initiation of PC-ECLS occurs in <4% of patients [2]. Transitioning to ECLS support during the index operation can be accomplished using central or, preferably, peripheral cannulation (see Sections 8 and 10), if no vascular contraindication exists.

10.1 Sternum management

Conversion to ECLS from CPB can be as simple as attaching the ECLS circuit to existing cannulae. Central cannulation generally requires the primary sternal incision to be left open, which may

REPORT

Downloaded from https://academic.oup.com/ejcts/article/59/1/12/5918808 by guest on 08 February 2021

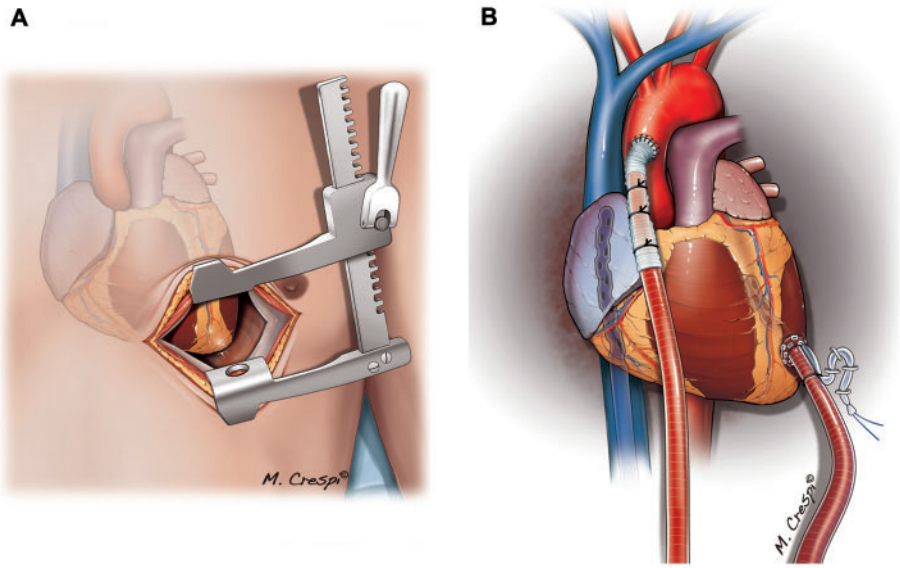

Figure 9: Veno-arterial configuration with a left minithoracotomy (**A**) approach and apical left ventricular venting cannulation (**B**). This configuration may allow full biventricular support, followed by a switch to isolated left ventricular support with removal of the venous cannula from the right atrium. The isolated support may be arranged, with or without the interpositioned oxygenator, for prolonged support (e.g. as bridge to durable left ventricular assist device as destination therapy or as bridge to a transplant).

be acceptable if a short duration of support is anticipated. Given that the increased bleeding risk is associated with an open-chest configuration, it is important to be aware that central cannulation can be configured in such a way as to allow chest closure. The potential advantages of sternal closure include minimization of blood loss, a theoretical reduction in the risk of infectious complications and an improvement in patient perioperative mobility. Disadvantages of sternal closure include an increased risk for tamponade and potential for cardiac compression from the cannulas themselves, if tunnelled to the subxiphoid region (Fig. 2).

Techniques to avoid cardiac compression included tunnelling cannulae superiorly and exiting the sternum at the level of the neck [105] via a transthoracic exit or the use of vascular grafts. The use of a vascular graft has the added advantage of avoiding the need for reopening the chest when decannulating [105, 106] (Fig. 10).

10.2 Inotropes, vasoconstrictors and steroids

The use of vasoactive, inotropic support remains a controversial issue in ECLS and particularly in PC-ECLS. Clearly, supporting cardiac contraction and improving ejection may be helpful to prevent intracardiac stasis [107, 108], but it is at the expense of myocardial work that may impede or delay recovery. The degree of vasoactive and inotropic support for these patients is unclear and rests on what is necessary to support cardiac ejection and prevent LV distension and stasis (see Left heart venting in Section 9).

10.3 Antibiotics

PC-ECLS is associated with an increased risk of a nosocomial infection [109]. The presence of an open chest and the circumstances surrounding the timing of cannulation undoubtedly influence this risk. Furthermore, a circuit heat exchanger maintains a uniform patient temperature that confounds infection monitoring. Prophylactic antibiotics are therefore recommended for all PC-ECLS patients from the operating room and while on ECLS as long as the chest remains opened plus an additional 24 h after chest closure. Prolonged antibiotic treatment while the patient is on ECLS might be considered under specific circumstances (after an acute endocarditis-related procedure or prolonged open-heart surgical procedures).

Although there is no clear correlation between prophylactic administration of antibiotics and a reduction in the risk of infection, given the wide variations in practice, administration of prophylactic antibiotics for up to 24 h with a closed chest is reasonable and in agreement with current ELSO guidelines [110].

10.4 Monitoring during intraoperative extracorporeal life support implantation

The following modalities are commonly used to guide the intraoperative management of the patient on ECLS:

10.4.1 Blood pressure pulsatility. Attention to arterial pressure pulsatility is critical in that lack of pulsatility may result in left-sided cardiac chamber distension or stasis, sometimes requiring intervention, either to drain the left side or to enhance LV contractility and ejection [71, 104]. Conservative actions (see Section 9; Figs 8 and 9) to support ejection and aortic valve opening should be instituted immediately. If this effort is unsuccessful, aggressive unloading procedures should be considered [101] (Figs 6–8). Clearly, if the LV is actively unloaded, the aortic valve will not open, there will be no ejection, but the problem of LV distension will have been appropriately addressed.

10.4.2 Peripheral arterial/pulse oximetry. In peripherally cannulated patients it is important to assure delivery of cerebral oxygen, which can be a mixture of retrograde ECLS blood and native CO. If the patient has poor native lung function, the

Downloaded from https://academic.oup.com/ejcts/article/59/1/12/5918808 by guest on 08 February 2021

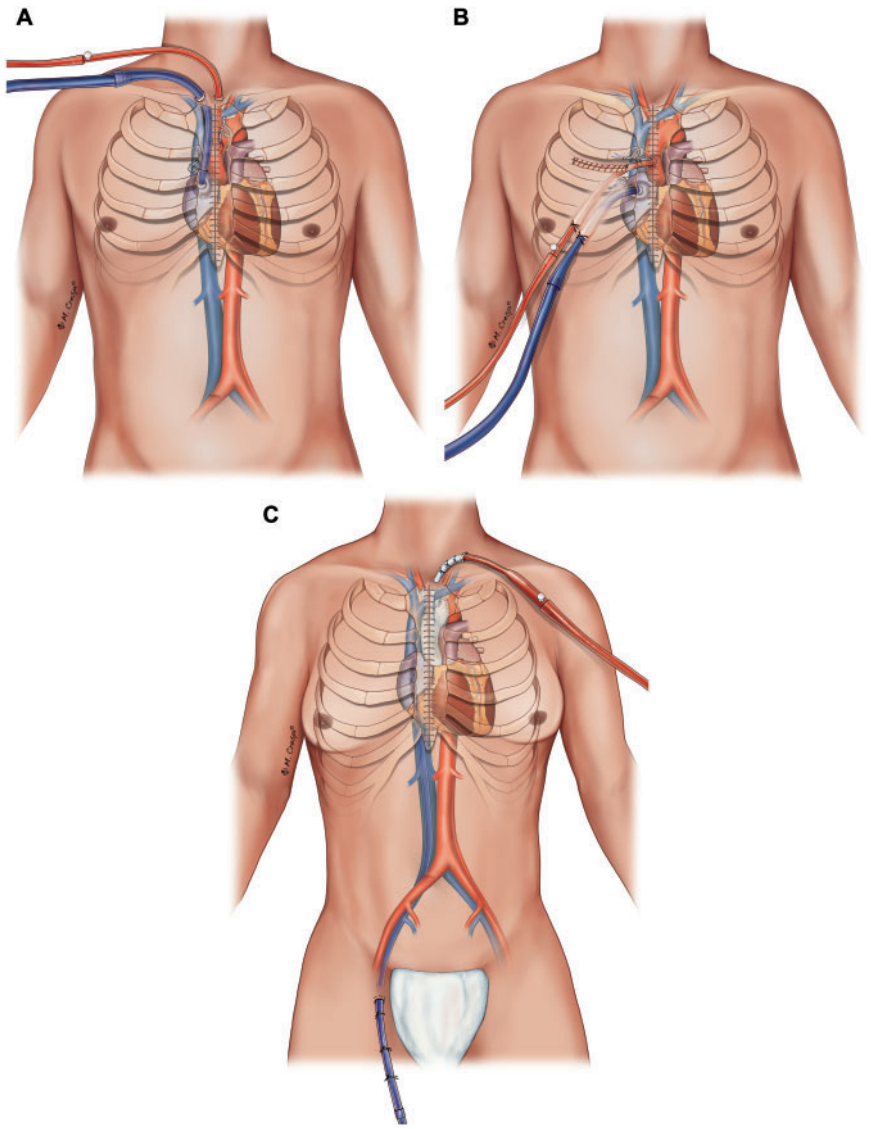

Figure 10: Alternative externalization of extracorporeal life support (ECLS) arterial and venous cannulae. (**A**) Jugular tunnelling of the arterial and venous cannulae at the jugular site, allowing sternal closure. (**B**) Externalization of the ECLS cannulae through intercostal spaces. (**C**) Externalization of the arterial outflow port of a veno-arterial ECLS through a prosthetic graft anastomosed at the aortic prosthesis; this approach may allow a central configuration, sternal closure and cannula withdrawal in case of weaning without reopening the sternum.

ejection of deoxygenated blood from the LV can result in hypoxic perfusion of the upper thorax, the coronary arteries and the brain, known as North-South or Harlequin syndrome or differential oxygenation. Recognize that for this phenomenon to occur, LV function must be of sufficient strength to override the aortic pressure generated by the inflow from the circuit, because if not, there will be no override of the aortic pressure and there will be no ejection of deoxygenated blood into the ascending aorta. Maintaining adequate right upper extremity oxygen saturation, although not a perfect reflection of adequate coronary oxygen delivery, ensures adequate cerebral oxygen delivery. This issue should not be a concern in centrally cannulated patients.

10.4.3 Pulmonary artery catheter. Pulmonary arterial and pulmonary capillary wedge pressures allow assessment of LV end-diastolic pressure and the possible need for ventricular unloading. The use of PA catheters varies among centres. Their placement may be difficult, but they may be helpful in diagnosing LV overload and distension as well as differentiating between cardiac and pulmonary causes of hypoxic respiratory failure.

10.4.4 Echocardiography. Echocardiography is routinely utilized to assess patients treated with PC-ECLS. Transoesophageal echocardiography allows determination of cannula positioning, cardiac chamber sizes, ventricular function and the need for venting. It is also a primary tool to evaluate Impella or other catheter placements (Section 8.3) [111].

10.4.5 Near-infrared spectroscopy. Near-infrared spectroscopy (NIRS), a non-invasive monitoring modality, allows assessment of adequate cerebral oxygen delivery. Although there is no consensus with respect to normal and abnormal thresholds,

Downloaded from https://academic.oup.com/ejcts/article/59/1/12/5918808 by guest on 08 February 2021

trends and asymmetry can signify important changes in cerebral perfusion, allowing timely intervention when dealing with a potential differential oxygenation or in detecting extremity malperfusion in peripheral ECLS [91, 112].

10.5 Description of the evidence

10.5.1 Peripheral arterial/pulse oximetry. The intraoperative assessment of right and left hand-based oximetry may immediately provide the level of the mixing point (heart and ECLS). This monitoring will play a larger role in management in the ICU (see Section 11).

10.5.2 Pulmonary artery catheter. The utility of pulmonary arterial catheters in patients on ECLS has not been studied prospectively, particularly in the operating room, but may provide useful information regarding LV unloading and help ECLS weaning in the future [113].

10.5.3 Echocardiography. Although the direct contribution of echocardiographic imaging to clinical care has not been prospectively evaluated, the breadth of information provided to the clinician has been recently highlighted [111]. Assessment of ventricular function is critical to decision-making about adequacy of LV unloading and weaning or the need to transition to alternative MCS [111] as discussed in the related sections.

10.5.4 Cerebral and lower limb near-infrared spectroscopy. Although there is no prospective trial on NIRS in ECLS patients, Wong *et al.* described their experience with a small cohort of patients [91, 112]. Among 20 patients who were monitored, all had significant decline (>25% from baseline) in cerebral saturations that triggered corrective manoeuvers. In 4 patients in whom cerebral desaturation persisted, all had evidence of intracerebral pathology upon further imaging. Further, 6 of these 20 patients had abnormalities identified by monitoring of their lower extremities that resolved with placing or replacing distal perfusion catheters [91]. More recently, Pozzebon *et al.* [112] reported their experience with NIRS monitoring in 56 patients with V-A ECLS. Significant cerebral desaturation occurred in 43 of these patients (74%), and these patients had a significantly higher incidence of acute cerebral complications and death. Although NIRS monitoring has not been shown to improve clinical results, it does appear to help identify patients who have complications, and it should be implemented from the initiation of ECLS.

Additional neurological monitoring, continuous or on demand, plays a critical role, particularly in the timely detection of potentially threatening complications during the ECMO run but is not immediately required when ECLS is initiated, as described in Section 12.

10.6 Reversal of anticoagulation and the management of major bleeding

Bleeding commonly complicates the care of a PC-ECLS-supported patient, most frequently in central cannulation, immediately post-bypass because coagulopathy often accompanies CPB [114]. In PC-ECLS, common practice includes discontinuation or reversal of heparin following cannulation and reintroduction of anticoagulation 24–48 h later, once haemostasis is achieved. ELSO guidelines recommend systemic heparinization adjusted by activated clotting time (ACT), activated partial thromboplastin time (aPTT), antifactor Xa or thromboelastography [115].

10.6.1 The evidence. As is discussed in Section 11, anticoagulation is required during prolonged ECLS to prevent circuit thrombus formation with embolization and/or circuit failure. However, bleeding remains the most frequent complication associated with ECLS. The incidence of bleeding is significantly higher in the PC setting and is related to the large open wound, exposed surgical suture lines and the usually long duration of CPB [31]. Additionally, many patients are transitioned directly from CPB to the ECLS circuit during full heparinization with ACT >400 s, eliminating any possibility for haemostatic control. Once they transitioned to ECLS, many centres adopted a strategy of partial heparin reversal with limited protamine administration [82]. Infusion of heparin is typically delayed until haemostasis is achieved, often within 24–48 h. Reports that suggest the safety of prolonged withdrawal of anticoagulation for as long as 3 days when faced with bleeding [116, 117] are important. The decision to reverse heparin and withhold anticoagulation is, of course, a balance of competing risks between bleeding and clotting. In practice, substantial mediastinal haemorrhage may persist despite reversal of heparin [6, 116, 118]. Mediastinal haemorrhage occurs even more frequently in patients who have an associated systemic inflammatory component, as may be seen in prosthetic endocarditis, ventricular assist devices and aortic dissection. ECLS support itself exacerbates coagulopathy even in the absence of systemic anticoagulation [119]. Determining the presence of any associated factor deficiency underlying the coagulopathy is a cornerstone of the management of PC bleeding. Laboratory testing, which may include ACT, aPTT, factor Xa activity, fibrinogen levels and thromboelastography, may guide therapy. Thromboelastography is frequently used to identify deficiencies in clotting mechanisms, thereby allowing targeted blood component replacement [120]. When massive bleeding is present, resuscitation should be administered in a 6:6:1 ratio of packed cells, fresh frozen plasma and platelets to avoid further dilutional coagulopathy [121]. In the most extreme cases, pharmacological agents like activated factor VII and prothrombin complex concentrate can be utilized, although the safety of these drugs remains uncertain in this setting [121]. Institution-specific protocols should be established for ECLS circuit management to address the potential need for rapid ECLS circuit replacement.

11. POSTOPERATIVE ANTICOAGULATION

11.1 Background

11.1.1 Heparin. Unfractionated heparin is the most widely used antithrombotic agent for anticoagulation during ECLS and is the anticoagulant of choice per the ELSO guidelines [115, 122]. It is not a direct anticoagulant but relies on its interaction with antithrombin (AT) III, increasing its avidity most notably for factor Xa and factor II (thrombin) by a factor of 10^3. Unfractionated

Downloaded from https://academic.oup.com/ejcts/article/59/1/12/5918808 by guest on 08 February 2021

Recommendations for intraoperative monitoring and antibiotic and anticoagulation management

Recommendations	Class[a]	Level[b]
Sternal closure		
Sternal closure should be considered to reduce bleeding and infectious complications.	IIa	C
Inotropes, vasoconstrictors, steroids		
It should be considered that inotropes are judiciously used to avoid LV stasis by promoting LV ejection.	IIa	C
In the presence of adequate oxygen delivery but with low systemic vascular resistance, vasoconstrictors may be considered to support blood pressure and counteract vasoplegia.	IIb	C
Antibiotic prophylaxis		
Perioperative short-term (24 h) antibiotic prophylaxis is recommended in patients on PC-ECLS [109].	I	B
Prolonged antibiotic coverage should be considered in central PC-ECLS with open chest until sternal closure.	IIb	C
Prolonged antibiotic coverage may be considered in peripheral PC-ECLS under specific circumstances (postacute endocarditis-related procedure, prolonged open-heart surgical procedures).	IIb	C
Monitoring		
It is recommended that intraoperative TOE be utilized to assess catheter placement and LV unloading.	I	C
The use of NIRS for both cerebral and extremity assessment of oxygenation to assure symmetry and to prevent subclinical ischaemia should be considered for the operating room in case of initiation of peripheral ECLS intraoperatively.	IIa	C
Anticoagulation for ECLS		
Reversing intraoperative heparin with protamine after CPB termination may be considered in patients with PCS.	IIb	C
Initiation of ECLS without heparin administration should be considered until bleeding is minimal in the postoperative phase.	IIb	C
In case of non-surgical massive bleeding, procoagulant interventions should be considered based on POC tests.	IIa	C
In case of life-threatening and refractory massive non-surgical bleeding, off-label use of rFVIIa may be considered.	IIb	C

[a]Class of recommendation.
[b]Level of evidence.
CPB: cardiopulmonary bypass; LV: left ventricular; NIRS: near-infrared spectroscopy; TOE: transoesophageal echocardiography; PC-ECLS: post-cardiotomy extracorporeal life support; PCS: post-cardiotomy shock; POC: point-of-care; rFVIIa: recombinant factor VIIa.

heparin has a half-life of 90 min and is made up of non-uniform complex glycosaminoglycans that bind to AT via a pentasaccharide sequence. Molecules of all sizes increase the avidity of AT for Xa, but only the larger molecules (approximately one-third of the total) potentiate the inhibition of thrombin [123]. By inhibiting thrombin and factor Xa, heparin also inhibits thrombin-induced platelet activation as well as the consequent activation of factors V and VIII [124]. Both the importance and a major drawback of heparin is the host's immune response, which can lead to heparin-induced thrombocytopaenia (HIT).

11.1.2 Direct thrombin inhibitors. Direct thrombin inhibitors (DTIs) are relatively short-acting anticoagulants that bind directly to thrombin, independent of any cofactors, with a predictable effect. They can inhibit bound thrombin, thereby preventing clot formation at the level of the clot itself, rather than only having the capability of inhibiting free thrombin, as is the case with heparin. Finally, unlike heparin, DTIs do not generate an immune-mediated response, as with HIT.

Bivalirudin has a short elimination half-life (25 min), is 80% metabolized directly when attached to thrombin, independent of kidney or liver function. Twenty percent is excreted renally, requiring dose adjustment in patients with renal insufficiency. *Argatroban*, on the other hand, is metabolized by the liver and has a half-life approximately twice that of bivalirudin. None of the DTIs have a specific antidote, but the short half-life of bivalirudin and the fact that it is relatively independent of organ-specific elimination (unlike argatroban) make it the preferred DTI. Unlike argatroban or heparin, the direct proteolysis of bivalirudin when attached to thrombin theoretically allows elimination of its anticoagulant effect, which results in clot formation. Intravascularly, e.g. intracavitary LV stasis, this can be life-threatening, but extravascularly, e.g. soft tissue haematoma or haemothorax, the loss of anticoagulant activity might be advantageous.

11.2 The evidence

11.2.1 Bleeding. Bleeding represents the most common complication in patients on PC-ECLS [31, 118]. Reoperation rates for bleeding after elective cardiac surgery are typically between 2% and 5%, whereas patients who require PC-ECLS have reoperation rates between 11% and 62%, although the rate is lower when a peripheral cannulation approach is used [41, 79]. These patients often require a significant quantity of blood products. This level of use increases the economic burden not only because of the cost of the blood products but also because of the complications associated with transfusions (lung and renal injury, immunocompromise with increased infections), which are known to be associated with more in-hospital deaths [125].

11.2.2 Commencement of postoperative anticoagulation. In the immediate postoperative period, all anticoagulation should be withheld until periprocedural bleeding has diminished (Section 10). When chest tube drainage is acceptable, e.g. <100 cc/h, within 24–48 h of cessation of CPB, anticoagulation can be resumed. Bolus dosing does not appear to be necessary. Heparin is the recommended drug of choice [115, 122], although, despite the lack of a reversal agent, bivalirudin may be an easier anticoagulant to manage and has been used effectively as an alternative to heparin

REPORT

Downloaded from https://academic.oup.com/ejcts/article/59/1/12/5918808 by guest on 08 February 2021

[126–131]. Despite the theoretical worry regarding bivalirudin-related proteolysis and the loss of anticoagulation in stagnant blood, which could result in unwanted clots, in practice this does not appear to be problematic. There are only sporadic case reports of the use of argatroban in ECLS, all showing effectiveness. The most significant disadvantage of these drugs is the lack of large prospective studies showing effectiveness. Thus, despite successful reports, their use in ECLS anticoagulation is 'off label' and is not recommended by the manufacturers for this purpose.

11.3 Monitoring of coagulation systems

The ELSO guidelines [115, 122] are currently non-committal on the subject of appropriate monitoring, saying, 'Ultimately, every ECLS programme will have to come up with an approach to monitoring the anticoagulant effect of unfractionated heparin that works best for their patients in their individual centre':

1. ACT measures the seconds needed for whole blood to clot upon exposure to an activator of an intrinsic pathway by the addition of factor XII activators. The normal ACT is 100–120 s.
2. aPTT measures the seconds needed for plasma (not whole blood) to clot upon exposure to calcium, phospholipid and an activator (silica or kaolin, usually). The clot is measured optically.
3. Heparin concentration (anti-Xa activity assay) measures antifactor Xa activity, i.e. the ability of a patient's plasma (containing heparin-AT III complex) to inhibit exogenously added factor Xa from hydrolyzing a synthetic substrate. Thus, the antifactor Xa assay evaluates the effect of heparin inhibition of this one enzymatic reaction, accurately determining heparin concentration but removed from its *in vivo* effect.
4. Thromboelastography is an assay that measures various components of blood coagulation, specifically the R value, which represents the time until first evidence of clot detection; the K value, the time from the first evidence of clot to a clot width of 20 mm; the alpha angle, which is the tangent to the curve describing clot formation taken at the K value; maximum amplitude, representing clot thickness or strength; and the LY30, a measure of clot lysis, as the decrement in the maximum amplitude at 30 min.
5. Ecarin clotting time (for DTI anticoagulation assessment) involves adding a known amount of ecarin (a proteolytic, procoagulant enzyme, isolated from snake venom) to plasma and measuring the time to clot formation. The DTIs prolong the ecarin clotting time in a linear fashion throughout pharmacological concentrations, unlike aPTT or ACT, and thus is a more reliable measure of DTI anticoagulation.
6. AT III levels, as the crucial cofactor to heparin, are measured to better understand heparin resistance.
7. Measures of haemolysis (inadequate anticoagulation): lactate dehydrogenase, plasma free haemoglobin, fibrinogen, factor 8 and d-dimer.

11.3.1 Evidence for monitoring guidelines. The management of anticoagulation has not been standardized. However, the effectiveness of heparin can be monitored using the ACT, targeting a level of 180–200 s [115, 132], or aPTT, targeting a prolongation to 50–80 s [133]. Other laboratory tests to determine anticoagulation are used in ECLS; however, target ranges and triggers for intervention for these tests are not uniform [132].

11.3.2 Heparin-induced thrombocytopaenia. Clinically diagnosed HIT occurs in only 1–3% of cases where heparin exposure continues postoperatively, with an associated mortality of 5% [130, 134]. The incidence is similar in patients with ECLS [131]. A DTI, specifically bivalirudin or argatroban, should be used as the alternative to heparin when HIT is being considered, both to halt the immunostimulation leading to thrombocytopaenia and to avoid the development of potentially lethal thrombotic thrombocytopaenia, with its associated mortality of 50% [130, 131, 134].

Recommendations for postoperative anticoagulation management

Recommendations	Class[a]	Level[b]
Heparin is recommended as the anticoagulant of choice for PC-ECLS.	I	C
If HIT is suspected, it is recommended to change anticoagulation to DTIs [130, 131, 134].	I	B
In the postoperative period, it is recommended to withhold anticoagulation until bleeding has diminished to acceptable levels.	I	C
It is recommended to monitor anticoagulation using the following tests: • ACT 160–220 s • aPTT 50–80 s	I	C
A TEG-driven algorithm should be considered for anticoagulation management.	IIa	C

[a]Class of recommendation.
[b]Level of evidence.
ACT: activated clotting time; aPTT: activated partial thromboplastin time; DTI: direct thrombin inhibitor; HIT: heparin-induced thrombocytopaenia; PC-ECLS: post-cardiotomy extracorporeal life support; TEG: thromboelastography.

12. INTENSIVE CARE UNIT MANAGEMENT DURING EXTRACORPOREAL LIFE SUPPORT

The goals of this section are to focus on selected areas that typically remain controversial to provide guidance in these areas rather than to provide a comprehensive discussion of ICU management.

12.1 Haemodynamics

12.1.1 Background. Patients who arrive in the ICU on ECLS after a cardiotomy are frequently malperfused for a period of time [135]. The goal of V-A ECLS is to provide cardiopulmonary support such that any end-organ ischaemia is reversed. In general, PC-ECLS is used as a bridge to recovery, not to a transplant or to a durable device; thus, every effort should be made to rest the heart as completely as possible to allow regenerative processes to occur.

Downloaded from https://academic.oup.com/ejcts/article/59/1/12/5918808 by guest on 08 February 2021

12.1.2 The evidence. Monitoring haemodynamics on ECLS has its nuances. Blood flow is not only measured by ECLS output but must also include that generated by LV ejection. Only in the case of no LV ejection are the ECLS and systemic CO similar. But with or without ejection, the use of central venous haemoglobin oxygen saturation or mixed venous oxygen saturation allows an estimate of the cardiac index. If the venous return is low in the inferior vena cava or common femoral vein, there will be 2 parallel circuits in the patient, and the Fick principle, which relies on central venous haemoglobin oxygen saturation or mixed venous oxygen saturation value, will be unreliable. In this situation, RV output estimated using echocardiography allows measurement of the CO, and when added to the CO from the ECLS circuit, allows determination of total systemic arterial flow.

At times, cannula size and/or placement, not intravascular volume, is the limiting factor for adequate ECLS flow. Therefore, repositioning of the venous line or placement of a second line may be required to improve drainage and allow for an increase in ECLS flow.

In patients whose LV is not vented, monitoring the systemic blood pressure pulsatility and the pulmonary diastolic or wedge pressure can help determine the adequacy of LV decompression and help distinguish primary pulmonary versus cardiac failure when faced with a falling P/F ratio (see Section 10.4). Furthermore, PA catheterization may be extremely helpful during the weaning process, allowing insight into myocardial function and its management [113, 136]. In the face of inadequate LV unloading, non-aggressive as well as aggressive, that is, catheter or device-based intervention, will be necessary [71, 101, 137] (see 'Left Heart Venting' in Section 9).

When administering fluid, there is no evidence that colloid volume resuscitation is superior to crystalloid, although it is more expensive [138].

For patients with RV failure, if no dedicated RV support system is in place, every effort should be made to decrease pulmonary vascular resistance. Full RV rest is possible with RA venous drainage as well as with venting the PA (Section 9). But, when RV ejection is occurring, direct pulmonary vasodilation can be achieved by using the lungs, or preferably, the 'sweep' to manipulate the pCO_2 <35 mmHg to create a mild to moderate respiratory alkalosis with a pH target of 7.45–7.5 [139]. Inhaled nitric oxide or epoprostenol may additionally lower pulmonary vascular resistance to decrease RV afterload and promote RV recovery.

For patients cannulated using the femoral artery, all arterial saturations should ideally be measured within the innominate artery distribution to ensure prompt diagnosis of the differential oxygenation. In this regard, NIRS can be enormously helpful in assessing asymmetrical cerebral perfusion [91, 112, 140]. Significant discrepancy in cerebral arterial oxyhaemoglobin saturation can be corrected by either preventing LV ejection or infusing oxygenated blood into the right atrium or PA by changing the configuration to a hybrid mode, as discussed in Section 7 [40, 49, 118].

Clinical examination, physiological monitoring and laboratory testing, including <5-cc difference in arterio-venous oxygen (i.e. a cardiac index combining native cardiac ejection as well as flow >2.5 l/min), urine output >0.5 cc/kg, sequential arterial blood lactate concentrations, liver function tests and creatinine and creatinine kinase levels, all reflect the adequacy of end-organ perfusion. A normal plasma lactate level suggests adequacy of tissue perfusion and has prognostic significance [34, 141].

Along with flow, blood pressure must be sufficient to perfuse, and although an exact target is not well established, a mean arterial pressure of 60–70 is usually considered adequate [142, 143]. Ideally, to maintain adequate renal perfusion, the mean arterial pressure-central venous pressure should be as normal as possible.

12.2 Left ventricular distension

As mentioned in Section 9, prevention of LV distension is critical to allow for myocardial recovery and to prevent further damage. Although radiological evidence of pulmonary oedema or frothy sputum might be the first clinical appearance of an elevation in LV end-diastolic pressure, monitoring of the extent of pulsatile systemic blood pressure and regular echocardiographic assessments of LV distension are the cornerstones to assess poor LV contractility, chamber size and dilatation. When distension occurs, efforts aimed at unloading the LV should be instituted as indicated in Section 9 (Figs 6–8).

12.3 Vascular and system-related complications

Limb perfusion impairment and local vascular complications occur frequently in peripheral ECLS [118]. Indeed, cannulation can be complicated by vessel injury/dissection, posterior vessel wall perforation, retroperitoneal haematoma/bleeding, arterio-venous fistula, pseudoaneurysm and compartment syndrome requiring fasciotomy, up to refractory limb ischaemia requiring amputation [118, 144]. The latter is devastating for patients and its incidence has been reported to be as high as 17% [144, 145]. Prevention of ischaemia to the leg ipsilateral to the femoral cannulation site can be accomplished by regular examination, including clinical assessment, Doppler scans and NIRS [146, 147]. In the presence of important bleeding at the cannulation site or ischaemia, decannulation with contralateral cannulation, switching to central or subclavian/axillary artery cannulation, in association with repair of vascular damage or thromboembolectomy or fasciotomy, are potential options in accordance with the severity of vascular injury or the type of complication [118]. Continuous surveillance (visual inspection and performance parameters) of the ECLS system and of the integrity and performance of the circuit (oxygenator dysfunction and leaking, circuit and vent line thrombosis, distal leg perfusion thrombosis) is mandatory.

12.4 Ventilation

12.4.1 Background. Ventilation practices in ECLS vary widely, but in PCS, for those patients receiving 'lung rest ventilation' to avoid high driving pressures in the face of poor lung compliance,

REPORT

Downloaded from https://academic.oup.com/ejcts/article/59/1/12/5918808 by guest on 08 February 2021

Recommendations for the prevention and management of postoperative complications associated with PC ECLS

Recommendations	Class[a]	Level[b]
In the face of LV distension, non-aggressive strategies (manipulating ECLS flow, vasodilation, increased PEEP) to promote LV unloading are recommended.	I	C
In case of LV distension non-responsive to non-aggressive strategies for LV unloading, catheter-based LV unloading or septostomy is recommended.	I	C
Withdrawal of anticoagulation in the face of bleeding may be considered with appropriate monitoring of (i) the oxygenator and pump circuit components for visual clot and adequate function; (ii) cerebral emboli; and (iii) LV stasis and clot.	IIb	C
It is recommended that native cardiac output with pump output is sufficient to perfuse all end organs, aiming for an arterio-venous oxygen difference of <5 ml O_2.	I	C
It is recommended that volume resuscitation with crystalloid is preferable to colloid (i.e. albumin) for initial volume resuscitation.	I	C
It is recommended that afterload, targeting MAP as well as ventricular distension, is minimized to improve myocardial recovery.	I	C
In patients with right heart failure, maintenance of pH between 7.45 and 7.5 using sweep should be considered to decrease pulmonary vascular resistance [139].	IIa	B
Pulmonary artery catheterization may be considered in all cases to assure adequate LV unloading and distinguish respiratory from cardiac failure.	IIb	C
Continuous surveillance (visual inspection and performance parameters) is recommended regarding the ECLS system and circuit integrity and performance (oxygenator dysfunction and leaking, circuit and vent line thrombosis, distal leg perfusion thrombosis).	I	C

[a]Class of recommendation.
[b]Level of evidence.
ECLS: extracorporeal life support; LV: left ventricular; MAP: mean arterial pressure; PC: post-cardiotomy; PEEP: positive end expiratory pressure.

the following recommendations in the ELSO Red Book pertain [110]:

1. Limit plateau pressures to <30 cm of water.
2. Use positive end expiratory pressure of 10–15 cm.
3. Set pressure control at 10 above the positive end expiratory pressure.
4. Set the respiratory rate at 10.

12.4.2 The evidence. In those patients who are actively ventilated and who are ejecting, it is important to manage ventilation settings so as to assure an appropriate pO_2 in the ascending aorta, avoiding differential oxygenation i.e. Harlequins or North-South Syndrome. However, in those patients with an acute lung injury who cannot adequately ventilate or oxygenate, prevention of LV ejection, particularly in patients peripherally cannulated, is necessary to prevent differential oxygenation and cerebral hypoxia. In these situations, lung protective strategies include low tidal volume (<6 cc/kg) with low peak airway pressures (<30 cm H_2O) and the avoidance of toxic FiO_2 concentrations (<40% has been shown to diminish the risk of ARDS) [148, 149]. The evidence that lung protective ventilator strategies improve outcomes in the general ICU population should apply to the PC-ECLS population as well.

Recommendations for ventilation strategies

Recommendations	Class[a]	Level[b]
Lung protection strategies employing low volumes, minimal barotrauma and low oxygen concentration are recommended [148, 149].	I	B
In peripheral V-A ECLS, early tracheostomy may be considered safe [152].	IIb	B
Routine bronchoscopy may be considered for diagnosis of pneumonia, clearing of secretions and evaluation of atelectasis and bleeding.	IIb	C

[a]Class of recommendation.
[b]Level of evidence.
ECLS: extracorporeal life support; PCS: post-cardiotomy shock; V-A: veno-arterial.

Although extubation practices in patients on ECLS are increasing [150], in many cases they are not applicable to PCS, where some patients will be centrally cannulated and weaned from ECLS in <6–7 days [33, 151]. In peripheral cannulation, an early tracheostomy does not appear to lead to increased mediastinitis [152]. However, given the risk associated with a tracheostomy in an open chest, patients should probably avoid it, if possible. Routine bronchoscopy is recommended to clear secretions and to evaluate for infection, pulmonary haemorrhage and atelectasis [153].

12.5 Infections

12.5.1 Background. The vulnerability to infection of the V-A ECLS patient in PCS with multiple cannulation sites, on a ventilator, often with an open chest, cannot be overemphasized. When one considers that the incidence of postoperative infections in patients having cardiac surgery is of the order of 3–4%, the risk of infection in ECLS is an order of magnitude greater, ranging from 9% to 65% [118, 154, 155]. The most common infections are bloodstream infections (3–16%), lower respiratory tract infections (24.4 episodes/1000 days) and surgical site infections (0.6–14.7%) [79, 156, 157]. Of note, infectious complications have also been associated with mechanical dysfunction of the ECLS circuit due to the activation of the coagulation cascade, leading to circuit clotting [156].

Downloaded from https://academic.oup.com/ejcts/article/59/1/12/5918808 by guest on 08 February 2021

Recommendations for prevention and treatment of ECLS-associated infections

Recommendations	Class[a]	Level[b]
For peripheral ECLS, prophylactic antibiotic administration is not recommended [109, 158].	III	B
In central ECLS with an open chest, prolonged prophylactic antibiotic coverage (including yeast) should be considered until 24 h after sternal closure is achieved.	IIa	C
Daily chlorhexidine sponge baths are recommended [160].	I	A
It is recommended that sepsis is treated according to institutional sepsis guidelines.	I	C
It is recommended that empiric antibiotics are discontinued early to decrease the incidence of resistant organisms.	I	C
It is recommended that antibiotic serum levels are used to guide dosing [162].	I	B

[a]Class of recommendation.
[b]Level of evidence.
ECLS: extracorporeal life support.

12.5.2 The evidence. It is estimated that one-third of patient deaths in PC-ECLS are directly attributable to infections [154]. There is limited evidence that antibiotic prophylaxis is of benefit, although no prospective studies effectively address this question [109]. Even in patients with central cannulation and an open chest, there is no evidence that prophylaxis is beneficial. Nevertheless, it must be acknowledged that in patients with open chests, the incidence of mediastinal wound infections is increased [158]. Finally, because the causative organisms are heterogeneous, gram-positive, gram-negative as well as fungal, only broad-spectrum antibiotics can be justified, should one choose to administer them. Given a lack of guidance of medical societies and a wide range of approaches to the prevention of infections, recommendations can only be based on expert opinion [159]. During the course of support of the patient on ECLS, infection should remain as a possibility and should be considered daily. Of importance is the fact that the ECLS circuit maintains body temperature as a result of its ability to heat or cool the outflow to the patient, and thus drastically diminishes the sensitivity of body temperature to reflect infection. Infection prevention should focus on the application of the VAP care bundle [155], chlorhexidine baths [160] and daily assessments of cannulation sites and central line dressings to maintain a blood-free, occlusive dressing [160]. Narrowing of the antibiotic spectrum based on culture results is a tenet of antibiotic therapy and diminishes the risk of the development of multidrug resistant organisms [161, 162].

12.6 Management of renal function

12.6.1 Background. Renal failure requiring renal replacement therapy (RRT) commonly occurs in 35–74% of patients undergoing PC-ECLS, a morbidity associated with an increase in mortality [2, 6, 33].

Recommendations for management of renal functions

Recommendations	Class[a]	Level[b]
Circuit access should be considered preferable to central venous access for the performance of dialysis in patients on ECLS.	IIa	C
Ultrafiltration rather than diuretics should be considered for volume removal.	IIa	C
It is recommended that serum drug levels are drawn in patients on ECLS complicated by renal failure [166, 167].	I	B

[a]Class of recommendation.
[b]Level of evidence.
ECLS: extracorporeal life support.

12.6.2 The evidence. The high incidence of renal failure in reported studies may reflect institutional bias regarding the timing of RRT, but undoubtedly the high rates of acute kidney injury associated with PCS almost certainly relate to prolonged CPB and shock prior to its initiation [163]. Patients without RRT showed a 3-month survival of 53%; the survival of patients with acute kidney injury requiring RRT was 17%. Longer duration of RRT was associated with more deaths [164, 165].

Indications for dialysis are no different than for any other critically ill patient, triggered by acidosis, electrolyte imbalances, volume overload and uraemia. However, ultrafiltration without dialysis may play a role in patients on PC-ECLS, because the volumes required to resuscitate these patients can be substantial and, depending on native kidney function for its removal, may be inadequate.

As is the case with ECLS in general, renal failure complicates the calculation of drug levels, and volumes of distribution can be challenging to predict [166, 167]. When appropriate, e.g. as with antibiotic dosing, serum levels should be followed rather than attempting to predict levels based on standard nomograms.

The method for performing dialysis is straightforward, either via percutaneous, central venous access or using the ECLS circuit, with dialysis inflow pressurized by the post-pump ECLS line. Whether via a central line or the circuit, care not to entrain air is crucial to avoid an air embolus and the need to emergently change out the circuit [168].

12.7 Central nervous system monitoring

12.7.1 Background and evidence. Neurological complications are devastating in any setting, but they are of particular concern in V-A ECLS. Approximately 15% of patients suffer a central nervous system complication, including brain death, cerebral infarction, haemorrhage and diffuse ischaemic brain injury-related seizures, with an associated mortality of close to 75–90% [169–171].

The cause of acute brain injury in patients on PC-ECLS is multifactorial, including surgery-related factors, thromboembolic

Downloaded from https://academic.oup.com/ejcts/article/59/1/12/5918808 by guest on 08 February 2021

Table 5: Criteria and clues for weaning from veno-arterial ECLS (modified from ELSO Red Book [110])

Types of ECLS systems	Criteria for weaning
V-A ECLS	Stable haemodynamic conditions for at least 24 h
	Mean arterial pressure >60 mmHg in the absence of or with low levels of vasopressors/inotropes
	Low arterial lactate levels (<2 mmol/l)
	PaO_2 >100 mmHg with ECLS FiO_2 <21% and FiO_2 40% on the mechanical ventilator
	Aortic flow velocity time integration >10–12 cm at an ECLS flow of 1–1.5 l/min
	Left ventricular ejection fraction >20–25%
	Doppler lateral mitral annulus peak systolic velocity ≥6 cm/s
	LV and RV adequate contractile response to volume challenge
	Venous and arterial patency and lack of distal thrombi should be checked after decannulation
	Use of other temporary assist device, like a transaortic suction device, may be used to enhance weaning from ECLS
	Transition to a VAD may be considered once haemodynamic stability has been achieved; however, in the presence of liver dysfunction, systemic inflammation or obesity, mortality will be high
From Oxy-RVAD ECLS (isolated RV support)	No sweep gas flow to the oxygenator for at least 2 h and maintain acceptable systemic arterial O_2 saturation (>90%) with normal respiratory parameters
	Stable haemodynamics with low doses of inotropes for at least 24 h
	Weaning trial should parallel prophylactic inotropic infusion (levosimendan)
	No signs of liver (transaminase increase) or renal (oliguria, anuria) stasis or evidence of steady and/or marked decrease
	TAPSE >10 mm with ECLS flow at 1–1.5 l/min
	Off-pump long-axis/short-axis ratio <0.55
	Lack of thrombi at the pulmonary artery level should be checked after decannulation

ECLS: extracorporeal life support; ELSO: Extracorporeal Life Support Organization; LV: left ventricle; Oxy-RVAD: right ventricular assist device with oxygenator; RV: right ventricle; TAPSE: tricuspid annular plane systolic excursion; V-A: veno-arterial.

Table 6: Criteria related to ECPR outcomes (adapted from Michels *et al.* [225] with permission from the authors)

Favourable for ECPR	Unfavourable for ECPR
Observed cardiac arrest	Unobserved cardiac arrest
Presumed cardiac aetiology, especially defibrillate initial heart rhythm	Age >75 years and frailty
No-flow time ≤5 min	No-flow time ≥10 min
Short low-flow time ≤60 min	Inadequate resuscitation measures
Consistently high-quality resuscitation measures	Clinical signs of severe irreversible brain damage or expected poor neurological prognosis
Presence of a reversible cause of the cardiac arrest (4 Hs and HITs): includes hypoxia, hypovolemia, hypo- and hyperkalemia (metabolic dysfunctions), accidental hypothermia, pericardial tamponade, thromboembolism (myocardial infarction, pulmonary embolism) and tension pneumothorax	Prolonged CPR of >20 min in the case of asystole (exception: accidental hypothermia, intoxication and suspected pulmonary embolism) or of >120 min in the case of persistent ventricular fibrillation/ventricular tachycardia
	Low pH (<6.8) and high lactate level (>20 mmol/l). Clinical signs of severe irreversible brain damage or expected poor neurological prognosis
	Patient's refusal (advance directive, the presence of emergency sheet regarding advance-care planning)
	Contraindications to full anticoagulation (e.g. active bleeding, severe trauma or haemothorax after CPR)

CPR: cardiopulmonary resuscitation; ECPR: extracorporeal cardiopulmonary resuscitation; HIT: heparin-induced thrombocytopaenia.

events, systemic anticoagulation and haemodynamic instability with cerebral hypoperfusion [169, 170]. If clinical suspicion arises, it is possible that early catheter-based intervention may offer some opportunity for rescue in patients with ischaemic events. Haemorrhagic events have no realistic interventions. Thrombolysis is contraindicated for cerebral ischaemic events in the PC setting. Optimization of anticoagulation and passive/active rehabilitation is also important [118].

12.7.2 Electroencephalography and somatosensory evoked potential. Electroencephalography (EEG) has been extensively studied in paediatric patients on ECLS but little is known about its utility in adult patients. Because the neurological status of many ECLS-supported patients is in question, EEG could potentially provide important diagnostic as well as prognostic information, playing a pivotal role in the timely detection of acute brain injury in ECLS [170, 172, 173].

Downloaded from https://academic.oup.com/ejcts/article/59/1/12/5918808 by guest on 08 February 2021

Recommendations for central nervous system monitoring

Recommendations	Class[a]	Level[b]
CT imaging is recommended to diagnose acute brain injury in comatose patients, if transportable.	I	C
EEG and SSEP are recommended to diagnose acute brain injury in comatose patients.	I	C
Cerebral NIRS monitoring should be considered to decrease inadvertent hypoxic cerebral perfusion.	IIa	C
Transcranial Doppler monitoring for embolic signals may be useful to guide anticoagulation or circuit component changeouts.	IIb	C

[a]Class of recommendation.
[b]Level of evidence.
CT: computed tomography; EEG: electroencephalography; NIRS: near-infrared spectroscopy; SSEP: somatosensory evoked potential.

12.7.3 Computed tomography imaging. Computed tomography assessment for an acute brain injury (along with lung, bowel or other organ- or system-related complication) is recommended in cases of clinical suspicion as long as the risk associated with patient transport to the radiology suite is not prohibitive.

12.7.4 Near-infrared spectroscopy. Few studies have examined the therapeutic efforts to decrease the incidence of brain injury post-ECLS initiation. Application of NIRS technology may be helpful to assure cerebral perfusion, as mentioned previously, and particularly important in peripherally cannulated ECLS patients in whom the differential oxygenation in relation to cerebral perfusion may exist [91, 112, 140].

12.7.5 Transcranial Doppler. In V-A ECLS patients, transcranial Doppler signals may show embolic signals; these signals are seen only occasionally in V-V ECLS and are often associated with visible oxygenator clots [173]. No long-term follow-up in these patients has occurred, and the clinical significance of these embolic signals is unknown. However, if they prove to be clinically relevant, improved anticoagulation and less tolerance of visible oxygenator clots may be possible therapeutic approaches.

13. WEANING, TRANSITION AND OUTCOMES

13.1 Weaning modalities and monitoring

Successful weaning from PC-ECLS ranges from 31% to 76% in published series, with almost half of the experiences showing a weaning rate at or slightly above 50%. As with ECLS for other indications, the survival to discharge is less encouraging, ranging

Recommendations for weaning and transition or termination in PC-ECLS

Recommendations	Class[a]	Level[b]
Weaning modalities and monitoring		
It is recommended that the aetiology of heart failure is compatible with recovery in PC-ECLS patients being considered for support weaning.	I	C
Medical optimization with evidence of end-organ recovery and correction of metabolic disturbances prior to consideration of weaning from ECLS are recommended.	I	C
TTE or TOE is recommended to assess valvular function and the degree of biventricular recovery during weaning trials.	I	C
Myocardial assessment and recovery algorithms are recommended.	I	C
Decannulation should be considered using systemic anticoagulation according to a standardized protocol.	IIa	C
It is recommended that extremity perfusion is assessed in all patients following decannulation and vascular intervention.	I	C
Transition or termination in PC-ECLS		
It is recommended that goals of care are established early and discussed with the patient's family and health care proxy. This discussion has to include the concept of medical futility and a plan to terminate support in this event.	I	C
Ethics and palliative care consultations are recommended in counselling the care team or patient's families when ambiguity is present or to define goals of care better.	I	C
It is recommended that patients who fail to wean be considered for transition to intermediate or long-term MCS if there are no contraindications.	I	C
Transition to VAD may be considered if haemodynamic stabilization is achieved; however, in the presence of liver dysfunction, inflammatory status, female gender and obesity mortality will be high.	IIb	C
Patients fulfilling the eligibility criteria should be considered for HTx and VAD.	IIa	C
Transitioning to V-V ECLS should be considered when pulmonary dysfunction persists despite the recovery of cardiac function.	IIa	C

[a]Class of recommendation.
[b]Level of evidence.
ECLS: extracorporeal life support; HTx: heart transplant; MCS: mechanical circulatory support; PC: post-cardiotomy; TOE: transoesophageal echocardiography; TTE: transthoracic echocardiography; VAD: ventricular assist device; V-V veno-venous.

REPORT

Downloaded from https://academic.oup.com/ejcts/article/59/1/12/5918808 by guest on 08 February 2021

from 16% to 52%, with most centres reporting rates below 40%. These results suggest that consideration should be given to transitioning rather than weaning select patients when the possibility of durable cardiac recovery is remote. The goals of PC-ECLS are to restore end-organ perfusion, allow for correction of metabolic disturbances and avoid the toxicities of vasoactive drugs, all the while allowing for myocardial rest and recovery. The likelihood of achieving these goals varies greatly from patient to patient, and decisions regarding bridge-to-recovery versus bridge-to-transition strategy are ideally made early in the course of treatment. In either scenario, adequate ventricular unloading is an important component to promote myocardial recovery and to avoid progressive pulmonary congestion. The adequacy of support and central unloading is therefore of paramount importance to a successful recovery or transition strategy.

A bridge-to-recovery strategy is employed in the majority of PC-ECLS patients as long as the aetiology of cardiac failure is compatible with recovery. Several clinical indicators are useful for patient assessment, and recovery algorithms can be considered to guide practice.

Major metabolic disturbances such as lactic acidosis and liver injury should have resolved or demonstrated marked improvement prior to any attempt to wean the patient from ECLS. A patient on minimal inotropic support and low ECLS flow rates should have recovered a pulsatile arterial waveform, should be haemodynamically stable, with a baseline mean arterial pressure higher than 60 mmHg and should maintain adequate oxygen delivery and biventricular contractility, assessed by echocardiography, for at least 24 h (Table 4) [174, 175]. Pulmonary function should not be severely impaired. If PaO_2/FiO_2 is <100 mmHg when the FiO_2 of the ECLS gas flow is set at 21%, bridging the patient from V-A to V-V ECLS should be considered [174]. Patients who do not meet weaning criteria (Table 5) should be fully supported and allowed more time to recover. If this approach does not appear realistic, they should be considered for transitioning to longer term support or end-of-life preparations. Decannulation should be performed using systemic anticoagulation to allow for a trial of circuit clamping, which is recommended prior to cannula removal in case ECLS needs to be re-established. Cannulae should be removed soon after cessation and reversal of anticoagulation to avoid intravascular thrombosis. Small cannulae may not require vascular repair, and haemostasis can be achieved with prolonged pressure. Most often, direct arterial repair is required. Distal perfusion should be assessed in all patients following decannulation, and vascular intervention should be considered as appropriate. When a venous cannula is being removed, air can enter the venous blood through the side holes if the patient is breathing spontaneously. This is prevented by a Valsalva manoeuver on the ventilator or by short-term pharmacological paralysis.

13.2 Failure to wean, transition to ventricular assist device or heart transplant or termination

In select patients not expected to recover, consideration should be given to transitioning to an implantable or LT-MCS or, in rare cases, HTx. In these patients, the timing of the transition is influenced most by systemic factors and the patient's perceived ability to withstand a subsequent operation. Transitions when possible are best done early to avoid ECLS-related morbidity and infectious complications. Termination of ECLS for futility will need to be considered in patients without advanced therapeutic options who do not recover native function.

In acceptable candidates, transitioning to an intermediate or LT-MCS is best accomplished when end-organ function and neurological function have been restored, ideally within 1 week of ECLS initiation so as to minimize the risk of complications and patient deconditioning. Nevertheless, results with implantable LVADs are less favourable in V-A ECLS-supported patients [176]. The use of an LVAD may be considered in V-A ECLS patients once haemodynamics are stabilized. However, the presence of signs of liver dysfunction and inflammatory status as well as obesity (body mass index >30 $kg.m^2$), and female gender, portend a high mortality and, therefore, must be taken into account in the decision-making [177].

Rarely, a PC-ECLS patient is eligible for an HTx. Although in the USA <2% of patients receive a transplant after ECLS support in the current era [178], this practice is expected to become more common in the face of the new heart allocation system that took effect in 2018. To date, however, post-transplant survival in these patients is less favourable. In patients who are not candidates for long-term support or a transplant, ECLS should be discontinued promptly when the care team has determined medical futility and after discussion with the patient's family or health care proxy. The definition of futility may vary based on the expertise and resources of the institution. In each case, a reasonable deadline for organ recovery or replacement should be set early in the course of PC-ECLS. In most centres, 3–5 days of inadequate cardiac function in a patient who is not a VAD or transplant candidate is considered futile.

13.3 Early and long-term results

Outcome data related to PC-ECLS in adult patients are becoming increasingly available. As with most forms of ECLS support, appropriate patient selection and pre-ECLS end-organ function and injury are important determinants of clinical outcome. Reported end points may be broadly categorized as successful separation from ECLS, survival to hospital discharge and long-term survival. Some of the complications that occur during ECLS support represent significant morbidity and should also be considered when examining short- and long-term outcome results. No RCTs have been performed to demonstrate a survival benefit for the use of ECLS to support adult patients with PC cardiopulmonary failure. Indications for PC-ECLS are heterogeneous, and surgeons have differing thresholds for initiating it, all of which increase the difficulty of demonstrating an absolute survival benefit for its use. Furthermore, the survival advantage of ECLS used as a bridge to decision, to durable mechanical support device or to a transplant is not well established. When used as a bridge to transplant, waiting list and post-transplant survival appears to be worse than that observed in paediatric and adult patients supported with a non-ECLS ventricular assist device [179, 180]. However, published studies provide little information on clinical indications for ECLS versus VAD in these patients.

Downloaded from https://academic.oup.com/ejcts/article/59/1/12/5918808 by guest on 08 February 2021

13.3.1 Early results. Complications commonly occur during ECLS support, due to patient factors or as a direct result of ECLS therapy. Inherent heterogeneity in the adult PC-ECLS patient population prevents accurate and reproducible prediction of ECLS morbidity and mortality for individual patients. The duration of PC-ECLS support necessary for recovery of adequate myocardial function is typically 5–7 days. Data from many published series indicate that ∼40–60% of PC patients are successfully separated from ECLS support [2, 31, 70, 82, 85, 94, 95]. However, reported survival to hospital discharge ranges from ∼20% to 40% [2, 31, 70, 82, 85, 94, 95, 181]. Predictors of hospital mortality include pre-ECLS cardiopulmonary resuscitation, preoperative renal insufficiency, increased duration of CPB, perioperative lactate >4 mml/l and incomplete sternal closure [31, 69, 85]. Preoperative hepatic dysfunction (elevated levels of alkaline phosphatase and total bilirubin) has recently been identified as an independent predictor of reduced hospital and long-term survival in PC-ECLS patients [182]. ECLS factors associated with reduced survival include acute kidney injury requiring haemodialysis, elevated blood lactate level during ECLS support, bleeding and duration of ECLS support [16, 85, 98, 181]. Initial 24-h urine output after initiation of ECLS support has recently been identified as a reliable and easily measurable predictor of hospital survival and 2-year survival [183].

Although advanced age was historically considered a contraindication to ECLS support, the use of ECLS in patients >70 years of age has increased significantly during the past decade. Nevertheless, registry data and published series indicate that advanced age is associated with lower survival and an increased rate of neurological complications in patients who require V-A ECLS [16, 31, 156, 184]. However, the impact on survival is mitigated by patient demographics and comorbidities at the time of ECLS support [184]. A single-institution analysis of PC-ECLS reported that >50% of patients successfully separated from ECLS, with a hospital survival of 24.4% in patients ≥70 years of age, although these patients were almost twice as likely to die during the hospitalization period than patients aged 50–69 years [16].

13.3.2 Long-term results. Although a significant body of literature exists related to short-term/hospital survival of patients on ECLS, information on long-term survival is limited, particularly with PC-ECLS. Data from a large national database study suggest that PC-ECLS patients have a nine-fold increased risk of in-hospital mortality and are at increased risk for all-cause mortality and hospital readmission during the first year of follow-up compared with propensity score matched patients who did not receive ECLS [181]. However, survival, readmission rates and medical expenditures were similar from the second year of follow-up onward. Older age, advanced preoperative comorbidities and surgical complexity were associated with worse long-term survival. Acceptable long-term survival in PC-ECLS patients who survive to hospital discharge is supported by data from single-institution studies [16, 31, 85, 185]. For example, a single-institution study of a subgroup of patients who survived to discharge reported 88% survival at 1 year [54]. Additional single-institution studies have reported that most survivors had NYHA class I-II functional status during the long-term follow-up period [16, 69, 186].

14. ETHICS, FAMILY AND FUTILITY

14.1 Background

Long-term survival and quality of life are unpredictable in patients who require PC-ECLS. Fewer than 50% of adult PC-ECLS patients survive to hospital discharge [181], and many of these patients experience major complications [6]. Uncertainty of outcome, limited understanding of technology and increased decision-making and caregiving responsibilities cause acute psychological stress and strain in family members of adult ECLS patients. In many cases, family members continue to be impacted by the event and experience enduring symptoms consistent with post-traumatic stress disorder years later [187, 188].

14.2 Family relationships

In many cases, the clinical care team must balance a patient's clinical state, predicted clinical trajectory, documented or stated advanced directives and family wishes when deciding to escalate, de-escalate or withdraw care. With few exceptions, self-directed care decisions by PC-ECLS patients are generally not possible. Although the decision to initiate PC-ECLS support is made exclusively by the medical care team in a relatively acute setting, decisions regarding continuing and discontinuing support should include family member surrogates who may have limited medical knowledge and experience. Consequently, the care team should make a deliberate effort to provide close guidance of family members to help ensure, preemptively, that ECLS treatment decisions are consistent with patient preferences and goals of care [189]. Communication about risks, benefits and potential failures of ECLS support should be discussed as early as possible.

Family members should be updated on the patient's clinical status and invited to participate in daily care planning discussions. Realistic, evidence-based projections and expectations for meaningful survival and expected quality of life, as well as the therapies and technologies required to achieve them, should be re-evaluated at regular intervals and reviewed with family members [190, 191]. An approximate timeline for a reassessment of the balance of potential benefits and burdens should be established, including objective indicators of recovery and futility [192].

Recommendations for relationships with family members, futility and redirection of care

Recommendations	Class[a]	Level[b]
A shared decision-making model of care (including patient's family or relatives) is recommended.	I	C
It is recommended that an immediate advanced/palliative care team consultation is obtained for all patients on PC-ECLS.	I	C

[a]Class of recommendation.
[b]Level of evidence.
PC-ECLS: post-cardiotomy extracorporeal life support.

REPORT

Downloaded from https://academic.oup.com/ejcts/article/59/1/12/5918808 by guest on 08 February 2021

14.3 Futility

Discontinuation of ECLS support becomes appropriate when ECLS fails as a means to recovery, as a means to achieve candidacy for a transplant or as a transition to temporary or durable ventricular assist therapy. Members of the ECLS care team commonly favour decision-making authority for ECLS patients, reflecting physician hesitance to cede authority to presumably less knowledgeable family members [193]. Despite seemingly irrefutable evidence of medical futility, physicians may face conflicts with family members who oppose discontinuation of ECLS. Routinely incorporating members of an advanced/palliative care team within the overall patient care team may help guide difficult discussions and improve communication with families [194]. When engaging family members in discussions related to the futility of care, conversations should ideally focus on guiding surrogate decision makers within a framework of shared decision-making within their family as well as with the medical team [189–191, 193]. Unresolved conflicts regarding futility and decision-making related to discontinuation of support may require ethics consultations [189, 193].

Withdrawal of ECLS support should be undertaken when it has been determined that acceptable quality of life is not achievable, based on perceived or stated patient beliefs, or when the futility of the treatment has been determined. If not already involved with the patient's care, the advanced/palliative care team should be consulted to provide emotional and logistical support for family members [189, 194]. Appropriate sedative, anxiolytic and analgesic medications should be administered to the patient to prevent physical emotional discomfort.

15. EXTRACORPOREAL LIFE SUPPORT EDUCATION AND TRAINING

15.1 Background

Management of ECLS patients requires specific knowledge related to extracorporeal perfusion including commonly encountered simulation training [110, 195]. ECLS is a relatively uncommon event whose application requires experience, because complications associated with ECLS are varied and can be life-threatening. Complicating the issue of the need for experienced caregivers is that they are spread over a variety of disciplines, including respiratory therapy, nursing, surgery and critical care.

Recommendations for education and training

Recommendations	Class[a]	Level[b]
Didactic and water drills are recommended as a routine and repetitive part of ECLS training for providers [197].	I	B
ECLS simulation is recommended for ECLS multispecialty teams as well as individual specialists [195, 202].	I	B
ECLS simulation is recommended for team-based learning specialties [199–201].	I	B

[a]Class of recommendation.
[b]Level of evidence.
ECLS: extracorporeal life support.

15.2 How to teach extracorporeal life support

ELSO recommends training modules including didactics, water drills, animal laboratories, clinical exposure and written examinations [196]. A total of 17 specific topics are recommended as part of the curriculum, ranging from the history of ECLS to circuit components to cannulation techniques to complications, even encompassing the complicated overarching question of ethics. The ELSO Red Book [110] and the ECMO Specialist Training Manual [196] provide the knowledge base that covers the cognitive aspects of most of the issues involved in the utilization of ECLS.

Low- and high-fidelity simulation sessions appear to be effective in training health care professionals [194, 197, 198], and both set-ups are recommended for teaching ECLS teams. If the expense can be managed, trainees prefer high-fidelity simulation models [199–202] compared to basic didactics and water drills.

16. HUB-AND-SPOKE MODEL: TRANSPORT

16.1 Hub-and-spoke network

At its heart, the hub-and-spoke concept is predicated on the idea that institutions within a system have a well-defined role and understand their capabilities and limitations. Importantly, there should be clearly established triggers for transfer of a patient to a centre that may be better equipped to handle a particular problem. Throughout the health care community, this concept varies considerably by disease state (i.e. cancer, cardiovascular care and trauma) as well as from country to country. Established regionalized policies for cardiac surgery have been promoted in Canada and Great Britain. In contrast, the USA has no federal mandates regarding regionalization in cardiac surgery, although there has been ample debate on the subject [203]. As such, many US cardiac surgery programmes perform fewer than 200 cardiac surgical procedures annually. Because the incidence of PC failure remains <4% [2], the frequency with which these programmes may require the use of ECLS is invariably low. This situation is compounded by the fact that lower volume programmes are less likely to perform complex surgical procedures in high-risk patients who are more likely to develop PCS. As has been demonstrated in nearly every advanced medical treatment, there appears to be a strong association with hospital ECLS volume and outcome [204]. Additionally, many lower volume programmes do not have the established infrastructure to manage these patients without impacting the activities of other essential services (i.e. perfusion, blood bank). Transfer to an experienced and perhaps more resource-rich centre is both appropriate and should be encouraged. PCS is not always predictable based on the characteristics of the patient and the planned operation. It is inevitable that low-volume programmes, even when appropriately risk-averse, will require PC-ECLS. Furthermore, the nature of PCS requires immediate restoration of circulatory support; thus, the transfer of these patients without ECLS or other forms of MSC would be less desirable. It is incumbent upon both the tertiary referral centres and the smaller cardiac surgery programmes to create hub-and-spoke links in advance, thereby taking advantage of an

Downloaded from https://academic.oup.com/ejcts/article/59/1/12/5918808 by guest on 08 February 2021

established process rather than attempting to create one during a desperate situation. This approach also allows for guideline development and refinement and the creation of a sense of accountability on both sides of the transfer process. This transfer process is of utmost importance in patients theoretically eligible for transition to LT-MCS or an HTx. Therefore, a timely consult to discuss the case, immediate management (maybe also using remote imaging technology to better assess management options) and further short-term handling are of primary relevance to offer a full spectrum of more advanced treatment in potential candidates.

16.2 Patient transport

Whether transferring a patient on ECLS because of inexperience or insufficient resources or to provide access to transplant or durable LVAD capabilities, direct communication between transferring teams is essential to determine appropriateness of transfer and to clarify expectations. The transfer should be coordinated to ensure the safety of both the patient and the transport team. In the early period following initiation of PC-ECLS support, there may be substantial bleeding, risk of tamponade, wide variation in ECLS flow, high-dose inotropic and vasoactive infusions and worsening end-organ dysfunction. Transport should be delayed until reasonable haemostasis and haemodynamic stability have been achieved. As has been shown by many high-volume centres, once stable, patients can be safely transported by ground or air [205, 206]. An outstanding set of recommendations for the detailed logistics of the inter-hospital transport process is available at the ELSO website [207].

The essential elements for successful inter-hospital transport include trained personnel, an appropriately sized and tested vehicle, a transport-ready ECLS circuit, equipment to address cannulation or circuit emergencies, blood products and ACT and electrolyte point-of-care measuring devices. Advanced knowledge of the cannulation platform is important, and each cannula should be assessed for stability and proper fixation. As with any transport of critically ill patients, the receiving unit should be contacted immediately prior to departure with the estimated arrival time as well as granular details regarding infusions, ventilator settings, ECLS cannulation and flow, bleeding and other necessary resources.

Recommendations for inter-hospital transfer of PC-ECLS patients

Recommendations	Class[a]	Level[b]
ECLS patient transfer to an experienced ECLS centre should be considered if no established ECLS programme is present in the implant centre.	IIa	C
Timely contact with an experienced ECLS centre should be considered when an ECLS is indicated or in progress in centres without an established ECLS programme to discuss details about management and further options.	IIa	C

[a]Class of recommendation.
[b]Level of evidence.
PC-ECLS: post-cardiotomy extracorporeal life support.

17. THE IMPORTANCE OF A MULTIDISCIPLINARY TEAM

17.1 Team composition and credentialing

The first attempt to understand the level of specialization and experience exhibited within ECLS teams occurred in 1991 [208]. Multidisciplinary teams have included perfusionists, registered nurses and respiratory therapists as well as intensivists [208, 209]. Formal identification of ECLS teams has improved survival in recent retrospective studies [210–216]. In particular, a full-time intensivist team responsible for ECLS care appears to improve outcome substantially [217]. This finding is consistent with the knowledge that ICU staffing with the continual presence of physicians trained in critical care, ICU organization and rounds models improves outcomes [217, 218]. Though not in an ECLS population, the benefit of a pharmacist in daily rounds has been substantiated and should be strongly considered in team composition [212].

Given the difficulty in maintaining skills in multiple caregivers involving a variety of specialties for a procedure that is performed only rarely, hospitals have used 'hours of ECLS care per year' as a surrogate for adequate experience [208]. Clearly, the greater the number of team members within each field, the fewer the hours of care per year are experienced by each team member. A total of 75 h per year per team member has been used for credentialing in many hospitals performing ECLS [207].

17.2 Quality and performance improvement dashboards

Quality and clinical dashboards that provide summary data on ongoing performance metrics have the potential to improve

Recommendations for multidisciplinary team management

Recommendations	Class[a]	Level[b]
It is recommended that ECLS teams be supported by perfusionists, RNs or RTs with significant, ongoing experience, as determined by hours of ECLS care/year.	I	C
It should be considered that ECLS care teams be multidisciplinary and include a pharmacist [210, 211, 215].	IIa	B
It is recommended that full-time intensivists be members of the ECLS caregiving team [216, 217].	I	B
Hours of care per year of ECLS patients are recommended as a surrogate for maintenance of competency [207].	I	B
It is recommended that all ECLS programmes should have a quality and performance improvement committee that meets at least monthly.	I	C

[a]Class of recommendation.
[b]Level of evidence.
ECLS: extracorporeal life support; RN: registered nurse; RT: respiratory therapist.

REPORT

Downloaded from https://academic.oup.com/ejcts/article/59/1/12/5918808 by guest on 08 February 2021

care. Although the technique has been well described in the literature, meaningful changes in behaviour and quality of care have not been well demonstrated [214].

Nevertheless, every ECLS programme should have a quality assurance aspect to their programme, one which determines appropriate, accepted metrics by the multidisciplinary team. A quality assurance/performance improvement team involving all stakeholders should meet at least monthly to present outcomes and discuss the agreed upon dashboard with an eye to addressing procedural and structural issues in order to standardize care [215].

18. POST-CARDIOTOMY CARDIOPULMONARY RESUSCITATION WITH EXTRACORPOREAL LIFE SUPPORT

18.1 Background

In-hospital cardiac arrest complicates ~5% of adult cardiac surgery procedures. Many of these patients do not respond to routine resuscitative efforts and could benefit from ECLS [219]. Increasingly, cardiac surgery centres have dedicated ECLS teams capable of rapid decision-making and deployment. With the availability of miniaturized and mobile circuits, ECLS has become an important adjunct to select patients undergoing CPR, named extracorporeal cardiopulmonary resuscitation (ECPR). The application of ECLS to the PC surgical patient has not been widely reported. The 2015 update to the American Heart Association's advanced cardiovascular life support guidelines recognizes the utility of this modality but falls short of recommending its routine use [220].

18.2 Incidence

Despite its increasing application, results with ECPR have remained stagnant over time with survival to hospital discharge of 29% over 11 years in the ELSO registry [221]. In a recent single-centre, retrospective review, ECLS cannulation following a witnessed, in-hospital cardiac arrest was associated with the poorest survival. These patients comprised nearly 10% of their population and their survival to discharge was <14%, reflecting perhaps an overly aggressive use of this modality [222]. A French, single-centre study of patients who had ECPR over 10 years identified only 45 patients treated with ECLS for in-hospital cardiac arrest. Within this group, the overall survival to discharge was a disappointing 11.6%. Of 9 patients who arrested after cardiac surgery, none survived to discharge [223]. In another large US centre experience over 6 years, 23 patients suffered in-hospital arrest following cardiac surgery and were cannulated for ECPR. Seven of these patients survived to discharge, 6 of whom had a favourable neurological outcome (26%) [81]. Importantly, age appeared to significantly influence mortality: 71.4% of patients younger than age 50 survived to discharge versus 12.5% of older patients, with no patient older than 70 surviving the hospitalization.

Recommendations for PC-ECLS procedure

Recommendations	Class[a]	Level[b]
PC-ECPR should be considered in the setting of adequate CPR when the time from arrest to ECLS is <60 min.	IIa	C
It should be considered that centres performing cardiac surgery have a readily available ECPR team.	IIa	C

[a]Class of recommendation.
[b]Level of evidence.
CPR: cardiopulmonary resuscitation; ECLS: extracorporeal life support; PC-ECPR: post-cardiotomy extracorporeal cardiopulmonary resuscitation.

18.3 Setting and organization

There is a growing interest in the application of ECLS in the management of resuscitation of patients who suffer cardiac arrest. The post-cardiac surgery patient is part of a unique subset that might benefit from timely intervention. These patients are well known to the surgical team and generally reside in a closely monitored setting. In the report by Mazzeffi *et al.* [65], the majority of these patients arrested in the ICU and the remaining in the operating room or on the telemetry floor. Institution-specific guidelines and protocols seem prudent to minimize delays and maximize therapeutic benefit.

Present ELSO guidelines [224] support the recommendation of the American Heart Association for 'consideration of ECLS to aid CPR in patients who have an easily reversible event, and have had excellent CPR'. They further state that 'all contraindications to ECLS use . . . should apply to ECPR patients'. An ECPR consensus statement endorsed by several German medical societies addresses many of the debated issues [225].

These authors recommend consideration of a full-time ECPR team with ready availability and suggest that ECPR rescue is reasonable in favourable clinical scenarios [225]. They offer the criteria to assist in decision-making (Table 6).

Although ECPR outcomes in patients following cardiac surgery are disappointing, the use of ECLS is lifesaving in select patients. Cardiac surgeons will likely remain aggressive in providing whatever care is necessary to ensure their patients' survival. In this setting, it seems reasonable for centres to have prespecified teams, algorithms and inclusion criteria governing ECPR in postoperative cardiac surgery patients.

Patients emergently cannulated for ECLS following cardiac arrest should be given 30 000 U of intravenous heparin with an additional 10 000 U added to the circuit in accordance with the recent STS guidelines [24].

19. SPECIAL CONDITIONS

19.1 Background

Under certain circumstances, perioperative ECLS should be considered electively. The objective in this situation is not only to counteract anticipated, post-procedural cardiorespiratory compromise but also to address severe and refractory preoperative deterioration that could be expected with corrective surgery and with sufficient time to result in complete patient recovery.

Downloaded from https://academic.oup.com/ejcts/article/59/1/12/5918808 by guest on 08 February 2021

Recommendations for preoperative ECLS

Recommendations	Class[a]	Level[b]
The preoperative implantation of an ECLS system may be considered in patients with VSD with right or biventricular dysfunction and a short time from an AMI, particularly in the case of a posterior ventricular septal defect, with failure of IABP and pharmacological treatment.	IIb	C
The preoperative implantation of an ECLS may be considered in patients with extremely poor organ perfusion, acidosis or cardiac arrest to improve operative conditions (bridge to surgery), to enhance CPB management and weaning.	IIb	C
The implantation of an ECLS preoperatively may be considered in patients with refractory LCO in the presence of chronic and irreversible cardiomyopathy and potential candidates for a heart transplant or VAD implant (bridge-to).	IIb	C

[a]Class of recommendation.
[b]Level of evidence.
AMI: acute myocardial infarction; CPB: cardiopulmonary bypass; ECLS: extracorporeal life support; IABP: intra-aortic balloon pump; LCO: low cardiac output; VAD: ventricular assist device; VSD: ventricular septal defect.

19.2 Preoperative extracorporeal life support

The application of ECLS before the surgical procedure might be considered to stabilize high risk and unfavourable patient conditions, to provide preoperative circulatory support, to reverse the stress of shock and thereby to present the patient with a valuable option, allowing him or her to be a vastly improved surgical candidate.

In the presence of postacute MI ventricular septal defect, attending personnel usually aim at surgical delay to allow partial myocardial healing and fibrotic tissue formation, conditions that aid in achieving a successful outcome. In this setting, however, vasoactive and inotropic circulatory support, even with mechanical circulatory assistance, e.g. an IABP, as is currently recommended by guidelines [78], may not be sufficient to prevent further circulatory deterioration, forcing the procedure to be done earlier than what would be optimal. ECLS, which provides full cardiorespiratory support during this time period, might protect the patient's circulation while allowing time from infarction to the surgical correction, improving surgical outcomes [226, 227]. Experience in this area is still anecdotal, but the usefulness of ECLS in these circumstances, i.e. providing temporary support both preoperatively and postoperatively, to counteract RV/LV dysfunction refractory to pharmacological and IABP treatment, has significant appeal. Despite the attractiveness of applying ECLS in this manner, without further evidence, its efficacy and value in such a scenario must still be considered investigative.

Another scenario where ECLS might be anticipated to provide lifesaving support occurs when, preoperatively, a patient suffers acute circulatory collapse due to a surgically remediable diagnosis. In these conditions, despite the indication for surgery, highly compromised preoperative cardiopulmonary function with remarkably impaired peripheral perfusion accompanied by extreme acidosis and profound shock almost certainly jeopardizes the outcomes of even the most conventional open-heart procedures [228, 229]. In these cases, temporary cardiorespiratory support (specifically aimed at reversing oxygen debt with optimization of end-organ perfusion and gas exchange) may allow for significant improvement in the patient's condition, markedly decreasing the risk of the ensuing operation.

Preoperative ECLS already represents a well-recognized strategy in patients waiting for a heart transplant who present with acute, decompensated heart failure and cardiogenic shock, as either a bridge to a transplant or as a bridge to mechanical support bridging to a transplant [230]. In either situation, these patients have acceptable outcomes and represent the paradigm for ECLS as a bridge to definitive therapy. As one can easily recognize, and although it is not the topic of this paper, ECLS for acute, reversible, medical causes of cardiogenic shock is simply a parallel path afforded to patients as a result of this technological advancement in patient care.

19.3 Prophylactic extracorporeal life support

The preventive use of ECLS after cardiac surgery is gaining increasing attention in several aspects of surgical or interventional procedures. Indeed, as reviewed in this document, the use of prophylactic temporary support may find a place either preoperatively or perioperatively. These situations may address procedures in high-risk patients, either for general conditions or severely impaired cardiac contractility or in anticipation of a high-risk perioperative or periprocedural course.

The presence of severe, chronic preoperative cardiac or respiratory compromise prior to surgery is a well-known risk factor for a complicated or unfavourable outcome. The use of prophylactic IABP in high-risk patients in cardiac surgery has been shown to enhance the postoperative patient course [231]. However, in the presence of highly compromised conditions known to predispose the patient to a complicated perioperative course due to further cardiac or systemic jeopardy, a full and temporary cardiorespiratory support system might be useful to overcome and 'protect' the first crucial postoperative hours, thereby limiting further deterioration of metabolic imbalance and haemodynamic dysfunction, ultimately resulting in enhanced patient recovery and in the avoidance or limitation of complications.

Recommendation for prophylactic ECLS

Recommendation	Class[a]	Level[b]
The planned implantation of ECLS may be considered in patients with severe preoperative uni- or biventricular dysfunction to assist resuscitation and/or myocardial recovery.	IIb	C

[a]Class of recommendation.
[b]Level of evidence.
ECLS: extracorporeal life support.

Downloaded from https://academic.oup.com/ejcts/article/59/1/12/5918808 by guest on 08 February 2021

Recommendations for the use of ECLS in PC patients with VV ECLS, post-HTx or VAD implant

Recommendations	Class[a]	Level[b]
VV ECLS may be considered to support patients with severe refractory PC ALI.	IIb	C
ECLS should be considered as the preferred treatment option for severe PGD following an HTx [241, 244, 245].	IIa	B
ECLS may be considered an RVAD with an oxygenator to rescue patients with severe refractory RV failure following LVAD placement.	IIb	C

[a]Class of recommendation.
[b]Level of evidence.
ALI: acute lung injury; HTx: heart transplant; LVAD: left ventricular assist device; PC: post-cardiotomy; PGD: primary graft dysfunction; RV: right ventricular; RVAD: right ventricular assist device; VAD: ventricular assist device; VV ECLS: veno-venous extracorporeal membrane oxygenation.

In patients with severe RV or biventricular dysfunction undergoing emergency operations, a temporary PC-ECLS timely applied, avoiding an implant in emergency or unfavourable conditions (severe acidosis, refractory cardiogenic shock, renal-liver dysfunction and so forth), may represent a useful and effective strategic planning. Indeed, starting circulatory support in comfortable and logistically favourable conditions, i.e. intraoperatively, at the time of CPB weaning, may allow a smooth transition from the operation to ICU management, may require assistance for a short time and may allow prompt organ and patient recovery without the need to implement aggressive inotropic or other therapies potentially leading to further adverse events [232].

19.4 Veno-venous extracorporeal life support

Respiratory complications following cardiac surgery are a major cause of postoperative morbidity and mortality [233]. In the general population, acute lung injury is associated with a mortality rate approaching 40%. In the cardiac surgery population, the mortality rate has been reported as high as 80% in the most severe cases [234, 235]. The management of acute lung injury focuses on lung protective ventilation, following the demonstration of superior outcomes in the Acute Respiratory Distress Syndrome Network trial [160]. However, in severe stages of pulmonary dysfunction, these protective settings can fail to maintain adequate oxygenation. This situation has promoted the exploration of alternative rescue therapies, such as V-V ECLS. The Conventional ventilation versus ECLS for Severe Adult Respiratory failure (CESAR) trial substantiated the role of V-V ECLS in the treatment of severe and refractory ARDS with a higher 6-month survival in those treated with V-V ECLS compared with those managed conventionally [236]. However, the available literature on PC patients remains scarce. The incidence of V-V ECLS for severe PC acute lung injury has been reported to be between 0.5% and 1.5%, with survival to hospital discharge between 12% and 64% [237, 238].

As mentioned in Table 3, several configurations may be considered in PC patients to establish V-V ECLS in the presence of isolated respiratory dysfunction: Intraoperatively, a right atrium-to-PA or a right atrium-to-left atrium connection may be applied, whereas the more conventional double cannulation or single cannulation with a double-lumen cannula may be implemented in this situation.

19.5 Post-heart transplant extracorporeal life support (graft failure)

Primary graft dysfunction (PGD) is a life-threatening complication after an HTx. Its incidence varies between 3% and 30%, and PGD accounts for 40–50% of the early deaths seen after an HTx [239]. Severe PGD is classified as the need for MCS (other than an IABP) to maintain adequate end-organ perfusion following a transplant [240]. MCS can be provided by V-A ECLS or implantation of a temporary VAD. ECLS has been favoured historically due to ease of implantation and the ability to provide oxygenation. However, ECLS is associated with a variety of significant complications already described in this paper, but most notably in this scenario, undependable ventricular unloading and the problem of intracardiac blood stasis with clot formation [241, 242]. Alternatives, including temporary LVAD support, have more recently been considered, theoretically providing better LV unloading, using direct ventricular cannulation and capable of providing support for a longer period to allow cardiac recovery.

Survival to hospital discharge in patients who require ECLS support following HTx has been reported to be between 50% and 81% with acceptable long-term outcomes [243, 244]. Patients supported with ECLS following HTx have better short- and long-term outcomes with a lower rate of complications compared to patients supported with a VAD [244]. Moreover, in those who survive to hospital discharge, patients treated with ECLS have the same 1-year conditional survival as patients who do not have PGD [243]. Furthermore, patients requiring ECLS following HTx have lower mortality compared with patients who require ECLS support for all other aetiologies [245]. Although ECLS does provide adequate circulatory support, it has limitations related to LV unloading, durability and associated thromboembolic and vascular complications. In the face of a lack of myocardial recovery, more aggressive strategies may be required to salvage these patients, such as biventricular support, including a durable VAD or a total artificial heart [178].

19.6 Extracorporeal life support after a left ventricular assist device

Acute RV failure is a well-recognized, although rare, cause of morbidity and mortality following elective cardiac surgery (0.04–0.1%). However, it is a common complication following LVAD implantation with an incidence of 9–25% and a mortality rate varying between 19% and 83% [246]. Conventional management includes aggressive diuresis, inotropic support, pulmonary vasodilators and phosphodiesterase inhibitors. However, 10–15% of patients with severe RV failure refractory to conventional management require some form of MCS [247]. As described in Section 19.4, ECLS can be tailored to provide isolated RV support with (Oxy-RVAD) or without an oxygenator, e.g. by cannulating

Downloaded from https://academic.oup.com/ejcts/article/59/1/12/5918808 by guest on 08 February 2021

the femoral vein and the PA with a Dacron graft tunnelled under the right subcostal margin, allowing for chest closure [248, 249]. Gratefully, the use of ECLS as an Oxy-RVAD or simply with the RVAD mode following LVAD implantation is associated with a 30-day and 6-month survival of 86% and 60%, respectively, comparable to survival of patients who undergo LVAD placement and do not develop RV failure [248].

20. LIMITATIONS

This manuscript was conceived from the results of a broad literature search. However, due to the intrinsically limited evidence on the topic, several small case series, case reports or papers published more than 10 years ago have been included to provide a more extensive overview and provide relevant information. In particular, several important issues, like new approaches and trends, or information about several peculiar aspects (see LV unloading), had to be partially included because we could not find appropriate interpretation and discussion (such as the gender-specific differences) due to the limited consistency of the available literature.

21. CONCLUSIONS

PC-ECLS represents a valuable and an undisputedly precious tool in a cardiac surgery setting. Despite the enhanced technology of ECLS-related systems and increased experience, several aspects still deserve further investigation and improvement. Configuration and timing of implant are particular aspects that have received attention and have changed in recent years. Due to its aggressive use and other specific factors associated with ECLS, complications are frequent and sometimes life-threatening. The complex PC patient characteristics in the setting of ECLS are certainly responsible for unsatisfactory results; unfortunately, effective potential alternatives to what otherwise will be inevitable patient death are, at the moment, non-existent. The limited knowledge about body/organ and ECLS interaction and more extensive clinical/preclinical research represent high priority targets for additional studies. The patient-tailored approach, a reduced anticoagulation regimen or safer alternatives to heparin are all factors currently under assessment and will hopefully provide adjunctive advances to a nonetheless powerful, yet currently imperfect, ally in the PCS setting.

SUPPLEMENTARY MATERIAL

Supplementary material is available at *EJCTS* online.

ACKNOWLEDGEMENTS

The authors gratefully acknowledge the contribution of Massimiliano Crespi, who drew the anatomical illustrations present throughout the manuscript. In addition, they truly value the contributions of the peer reviewers whose valuable comments assisted them in achieving this goal.

FUNDING

This article was produced by and is under the sole responsibility of the EACTS, the ELSO, the STS and the AATS.

Conflict of interest: Roberto Lorusso: Consultant for LivaNova, and Medtronic, Advisory Board Member for Eurosets and PulseCath (all honoraria go to the hospital and university institutions for research funding). All other authors declared no conflict of interest.

REFERENCES

[1] Sousa-Uva M, Head SJ, Thielmann M, Cardillo G, Benedetto U, Czerny M *et al.* Methodology manual for European Association for Cardio-Thoracic Surgery (EACTS) clinical guidelines. Eur J Cardiothorac Surg 2015;48:809–16.
[2] Lorusso R, Raffa GM, Alenizy K, Sluijpers N, Makhoul M, Brodie D *et al.* Structured review of post-cardiotomy extracorporeal membrane oxygenation: part 1—adult patients. J Heart Lung Transpl 2019;38:1125–43.
[3] Stretch R, Sauer CM, Yuh DD, Bonde P. National trends in the utilization of short-term mechanical circulatory support: incidence, outcomes, and cost analysis. J Am Coll Cardiol 2014;64:1407–15.
[4] Maxwell BG, Powers AJ, Sheikh AY, Lee PH, Lobato RL, Wong JK. Resource use trends in extracorporeal membrane oxygenation in adults: an analysis of the Nationwide Inpatient Sample 1998-2009. J Thorac Cardiovasc Surg 2014;148:416–21.e1.
[5] Whitman GJ. Extracorporeal membrane oxygenation for the treatment of postcardiotomy shock. J Thorac Cardiovasc Surg 2017;153:95–101.
[6] Cheng R, Hachamovitch R, Kittleson M, Patel J, Arabia F, Moriguchi J *et al.* Complications of extracorporeal membrane oxygenation for treatment of cardiogenic shock and cardiac arrest: a meta-analysis of 1,866 adult patients. Ann Thorac Surg 2014;97:610–16.
[7] Broman LM, Taccone FS, Lorusso R, Malfertheiner MV, Pappalardo F, Di Nardo M *et al.* The Extracorporeal Life Support Organization Maastricht treaty for nomenclature: abbreviations for cannulation configuration in extracorporeal life support. A position paper of the Extracorporeal Life Support Organization. Crit Care 2019;23:36.
[8] Potapov EV, Crespo-Leiro MG, Combes A, Farber G, Hannan MM, Kukucka M *et al.* Expert consensus on long-term mechanical circulatory support. Eur J Cardiothorac Surg 2019;56:230–70.
[9] Keebler ME, Haddad EV, Choi CW, McGrane S, Zalawadiya S, Schlendorf KH *et al.* Venoarterial extracorporeal membrane oxygenation in cardiogenic shock. JACC Heart Fail 2018;6:503–16.
[10] Pitsis AA, Visouli AN, Burkhoff D, Dardas P, Mezilis N, Bougioukas G *et al.* Feasibility study of a temporary percutaneous left ventricular assist device in cardiac surgery. Ann Thorac Surg 2007;84:1993–9.
[11] Chamogeorgakis T, Rafael A, Shafii AE, Nagpal D, Pokersnik JA, Gonzalez-Stawinski GV. Which is better: a miniaturized percutaneous ventricular assist device or extracorporeal membrane oxygenation for patients with cardiogenic shock? ASAIO J 2013;59:607–11.
[12] Raffa GM, Gelsomino S, Sluijpers N, Meani P, Alenizy K, Natour E *et al.* In-hospital outcome of post-cardiotomy extracorporeal life support in adult patients: the 2007-2017 Maastricht experience. Crit Care Resusc 2017;19:53–61.
[13] McCarthy FH, McDermott KM, Kini V, Gutsche JT, Wald JW, Xie D *et al.* Trends in U.S. extracorporeal membrane oxygenation use and outcomes: 2002-2012. Semin Thorac Cardiovasc Surg 2015;27:81–8.
[14] Fux T, Holm M, Corbascio M, Lund LH, van der Linden J. Venoarterial extracorporeal membrane oxygenation for postcardiotomy shock: risk factors for mortality. J Thorac Cardiovasc Surg 2018;156:1894–902.
[15] Lorusso R, Cariou A, Flaatten H. The dilemma of patient age in decision-making for extracorporeal life support in cardiopulmonary resuscitation. Intensive Care Med 2019;45:542–4.
[16] Saxena P, Neal J, Joyce LD, Greason KL, Schaff HV, Guru P *et al.* Extracorporeal membrane oxygenation support in postcardiotomy elderly patients: the mayo clinic experience. Ann Thorac Surg 2015;99:2053–60.
[17] Lima EB, Cunha CR, Barzilai VS, Ulhoa MB, Barros MR, Moraes CS *et al.* Experience of ECMO in primary graft dysfunction after orthotopic heart transplantation. Arq Bras Cardiol 2015;105:285–91.
[18] Kittleson MM, Patel JK, Moriguchi JD, Kawano M, Davis S, Hage A *et al.* Heart transplant recipients supported with extracorporeal membrane oxygenation: outcomes from a single-center experience. J Heart Lung Transplant 2011;30:1250–6.
[19] Listijono DR, Watson A, Pye R, Keogh AM, Kotlyar E, Spratt P *et al.* Usefulness of extracorporeal membrane oxygenation for early cardiac allograft dysfunction. J Heart Lung Transplant 2011;30:783–9.

REPORT

Downloaded from https://academic.oup.com/ejcts/article/59/1/12/5918808 by guest on 08 February 2021

[20] 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.
[21] Haneya A, Philipp A, Puehler T, Rupprecht L, Kobuch R, Hilker M *et al.* Temporary percutaneous right ventricular support using a centrifugal pump in patients with postoperative acute refractory right ventricular failure after left ventricular assist device implantation. Eur J Cardiothorac Surg 2012;41:219–23.
[22] Argiriou M, Kolokotron SM, Sakellaridis T, Argiriou O, Charitos C, Zarogoulidis P *et al.* Right heart failure post left ventricular assist device implantation. J Thorac Dis 2014;6:S52–9.
[23] Zhao Y, Xing J, Du Z, Liu F, Jia M, Hou X. Extracorporeal cardiopulmonary resuscitation for adult patients who underwent post-cardiac surgery. Eur J Med Res 2015;20:83.
[24] Society of Thoracic Surgeons Task Force on Resuscitation After Cardiac Surgery. The Society of Thoracic Surgeons expert consensus for the resuscitation of patients who arrest after cardiac surgery. Ann Thorac Surg 2017;103:1005–20.
[25] Fukuhara S, Takeda K, Garan AR, Kurlansky P, Hastie J, Naka Y *et al.* Contemporary mechanical circulatory support therapy for postcardiotomy shock. Gen Thorac Cardiovasc Surg 2016;64:183–91.
[26] Zimmerman JE, Kramer AA, McNair DS, Malila FM. Acute Physiology and Chronic Health Evaluation (APACHE) IV: hospital mortality assessment for today's critically ill patients. Crit Care Med 2006;34: 1297–310.
[27] Schmidt M, Burrell A, Roberts L, Bailey M, Sheldrake J, Rycus PT *et al.* Predicting survival after ECMO for refractory cardiogenic shock: the survival after veno-arterial-ECMO (SAVE)-score. Eur Heart J 2015;36: 2246–56.
[28] Wang L, Yang F, Wang X, Xie H, Fan E, Ogino M *et al.* Predicting mortality in patients undergoing VA-ECMO after coronary artery bypass grafting: the REMEMBER score. Crit Care 2019;23:11.
[29] Poss J, Koster J, Fuernau G, Eitel I, de Waha S, Ouarrak T *et al.* Risk stratification for patients in cardiogenic shock after acute myocardial infarction. J Am Coll Cardiol 2017;69:1913–20.
[30] Samuels LE, Kaufman MS, Thomas MP, Holmes EC, Brockman SK, Wechsler AS. Pharmacological criteria for ventricular assist device insertion following postcardiotomy shock: experience with the Abiomed BVS system. J Card Surg 1999;14:288–93.
[31] Rastan AJ, Dege A, Mohr M, Doll N, Falk V, Walther T *et al.* Early and late outcomes of 517 consecutive adult patients treated with extracorporeal membrane oxygenation for refractory postcardiotomy cardiogenic shock. J Thorac Cardiovasc Surg 2010;139:302–11.
[32] Elsharkawy HA, Li L, Esa WA, Sessler DI, Bashour CA. Outcome in patients who require venoarterial extracorporeal membrane oxygenation support after cardiac surgery. J Cardiothorac Vasc Anesth 2010; 24:946–51.
[33] Wang L, Wang H, Hou X. Clinical outcomes of adult patients who receive extracorporeal membrane oxygenation for postcardiotomy cardiogenic shock: a systematic review and meta-analysis. J Cardiothorac Vasc Anesth 2018;32:2087–93.
[34] Li CL, Wang H, Jia M, Ma N, Meng X, Hou XT. The early dynamic behavior of lactate is linked to mortality in postcardiotomy patients with extracorporeal membrane oxygenation support: a retrospective observational study. J Thorac Cardiovasc Surg 2015;149:1445–50.
[35] Hausmann H, Potapov EV, Koster A, Krabatsch T, Stein J, Yeter R *et al.* Prognosis after the implantation of Intra-Aortic Balloon Pump in cardiac surgery calculated with a new score. Circulation 2002;106: 203–6.
[36] Toomasian JM, Schreiner RJ, Meyer DE, Schmidt ME, Hagan SE, Griffith GW, Barteltt RH *et al.* A polymethylpentene fiber gas exchanger for long-term extracorporeal life support. ASAIO J 2005;51:390–7.
[37] Philipp A, Arlt M, Amann M, Lunz D, Muller T, Hilker M *et al.* First experience with the ultra-compact mobile extracorporeal membrane oxygenation system in inter-hospital transport. Interact CardioVasc Thorac Surg 2011;12:978–81.
[38] Muehrcke DD, McCarthy PM, Stewart RW, Foster RC, Ogella DA, Borsh JA *et al.* Extracorporeal membrane oxygenation for postcardiotomy cardiogenic shock. Ann Thorac Surg 1996;61:684–91.
[39] Abrams D, Garan AR, Abdelbary A, Bacchetta M, Bartlett RH, Beck J *et al.*; for The International ECMO Network (ECMONet) and The Extracorporeal Life Support Organization (ELSO). Position paper for the organization of ECMO program in adults patients. Intensive Care Med 2018;44:717–29.
[40] Brasseur A, Scolletta S, Lorusso R, Taccone FS. Hybrid extracorporeal membrane oxygenation. J Thorac Dis 2018;10:S707–15.
[41] Raffa GM, Kowalewski M, Brodie D, Ogino M, Whitman G, Meani P *et al.* Meta-analysis of peripheral or central extracorporeal membrane oxygenation in postcardiotomy and non-postcardiotomy shock. Ann Thorac Surg 2019;107:311–21.
[42] Werner NL, Coughlin M, Cooley E, Haft JW, Hirschl RB, Bartlett RH *et al.* The University of Michigan Experience with veno-venoarterial hybrid mode of extracorporeal membrane oxygenation. ASAIO J 2016; 62:578–83.
[43] Saeed D, Stosik H, Islamovic M, Albert A, Kamiya H, Maxhera B *et al.* Femoro-femoral versus atrio-aortic extracorporeal membrane oxygenation: selecting the ideal cannulation technique. Artif Organs 2014; 38:549–55.
[44] Kanji HD, Schulze CJ, Oreopoulos A, Lehr EJ, Wang W, MacArthur RM. Peripheral versus central cannulation for extracorporeal membrane oxygenation: a comparison of limb ischemia and transfusion requirements. Thorac Cardiovasc Surg 2010;58:459–62.
[45] Mariscalco G, Salsano A, Fiore A, Dalen M, Ruggieri VG, Saeed D *et al.* Peripheral versus central extracorporeal membrane oxygenation for postcardiotomy shock: a multicenter registry, systematic review and meta-analysis. J Thorac Cardiovasc Surg 2019; doi:10.1016/j.jtcvs.2019.10.078.
[46] Massetti M, Gaudino M, Saplacan V, Farina P. From extracorporeal membrane oxygenation to ventricular assist device oxygenation without sternotomy. J Heart Lung Transplant 2013;32:138–9.
[47] Ius F, Sommer W, Tudorache I, Avsar M, Siemeni T, Salman J *et al.* Veno-veno-arterial extracorporeal membrane oxygenation for respiratory failure with severe haemodynamic impairment: technique and early outcomes. Interact CardioVasc Thorac Surg 2015;20:761–7.
[48] Biscotti M, Lee A, Basner RC, Agerstrand C, Abrams D, Brodie D *et al.* Hybrid configurations via percutaneous access for extracorporeal membrane oxygenation: a single-center experience. ASAIO J 2014;60: 635–42.
[49] Stohr F, Emmert MY, Lachat ML, Stocker R, Maggiorini M, Falk V *et al.* Extracorporeal membrane oxygenation for acute respiratory distress syndrome: is the configuration mode an important predictor for the outcome? Interact CardioVasc Thorac Surg 2011;12:676–80.
[50] Sorokin V, MacLaren G, Vidanapathirana PC, Delnoij T, Lorusso R. Choosing the appropriate configuration and cannulation strategies for extracorporeal membrane oxygenation: the potential dynamic process of organ support and importance of hybrid modes. Eur J Heart Fail 2017;19:75–83.
[51] Cheng R, Hachamovitch R, Makkar R, Ramzy D, Moriguchi JD, Arabia FA *et al.* Lack of survival benefit found with use of intraaortic balloon pump in extracorporeal membrane oxygenation: a pooled experience of 1517 patients. J Invasive Cardiol 2015;27:453–8.
[52] Ariyaratnam P, McLean LA, Cale AR, Loubani M. Extra-corporeal membrane oxygenation for the post-cardiotomy patient. Heart Fail Rev 2014;19:717–25.
[53] Bakhtiary F, Keller H, Dogan S, Dzemali O, Oezaslan F, Meininger D *et al.* Venoarterial extracorporeal membrane oxygenation for treatment of cardiogenic shock: clinical experiences in 45 adult patients. J Thorac Cardiovasc Surg 2008;135:382–8.
[54] Hsu PS, Chen JL, Hong GJ, Tsai YT, Lin CY, Lee CY *et al.* Extracorporeal membrane oxygenation for refractory cardiogenic shock after cardiac surgery: predictors of early mortality and outcome from 51 adult patients. Eur J Cardiothorac Surg 2010;37:328–33.
[55] Meani P, Gelsomino S, Natour E, Johnson DM, Rocca HB, Pappalardo F *et al.* Modalities and effects of left ventricle unloading on extracorporeal life support: a review of the current literature. Eur J Heart Fail 2017;19: 84–91.
[56] Nuding S, Werdan K. IABP plus ECMO—is one and one more than two? J Thorac Dis 2017;9:961–4.
[57] Thiele H, Jobs A, Ouweneel DM, Henriques JPS, Seyfarth M, Desch S *et al.* Percutaneous short-term active mechanical support devices in cardiogenic shock: a systematic review and collaborative meta-analysis of randomized trials. Eur Heart J 2017;38:3523–31.
[58] Sandhu A, McCoy LA, Negi SI, Hameed I, Atri P, Al'Aref SJ *et al.* Use of mechanical circulatory support in patients undergoing percutaneous coronary intervention: insights from the National Cardiovascular Data Registry. Circulation 2015;132:1243–51.
[59] Thiele H, Zeymer U, Neumann FJ, Ferenc M, Olbrich HG, Hausleiter J *et al.* Intraaortic balloon support for myocardial infarction with cardiogenic shock. N Engl J Med 2012;367:1287–96.

Downloaded from https://academic.oup.com/ejcts/article/59/1/12/5918808 by guest on 08 February 2021

[60] Thiele H, Zeymer U, Neumann FJ, Ferenc M, Olbrich HG, Hausleiter J *et al.* Intra-aortic balloon counterpulsation in acute myocardial infarction complicated by cardiogenic shock (IABP-SHOCK II): final 12 month results of a randomised, open-label trial. Lancet 2013;382: 1638–45.

[61] Roffi M, Patrono C, Collet JP, Mueller C, Valgimigli M, Andreotti F *et al.* 2015 ESC Guidelines for the management of acute coronary syndromes in patients presenting without persistent ST-segment elevation: task Force for the Management of Acute Coronary Syndromes in Patients Presenting without Persistent ST-Segment Elevation of the European Society of Cardiology (ESC). Eur Heart J 2016;37:267–315.

[62] Sousa-Uva M, Neumann FJ, Ahlsson A, Alfonso F, Banning AP, Benedetto U *et al.*; ESC Scientific Document Group. 2018 ESC/EACTS Guidelines on myocardial revascularization. Eur J Cardiothorac Surg 2019;55:4–90.

[63] Thiele H, Ohman EM, Desch S, Eitel I, de Waha S. Management of cardiogenic shock. Eur Heart J 2015;36:1223–30.

[64] Distelmaier K, Schrutka L, Binder C, Steinlechner B, Heinz G, Lang IM *et al.* Cardiac arrest does not affect survival in post-operative cardiovascular surgery patients undergoing extracorporeal membrane oxygenation. Resuscitation 2016;104:24–7.

[65] Mazzeffi MA, Sanchez PG, Herr D, Krause E, Evans CF, Rector R *et al.* Outcomes of extracorporeal cardiopulmonary resuscitation for refractory cardiac arrest in adult cardiac surgery patients. J Thorac Cardiovasc Surg 2016;152:1133–9.

[66] Smedira NG, Blackstone EH. Postcardiotomy mechanical support: risk factors and outcomes. Ann Thorac Surg 2001;71:S60–6.

[67] Pokersnik JA, Buda T, Bashour CA, Gonzalez-Stawinski GV. Have changes in ECMO technology impacted outcomes in adult patients developing postcardiotomy cardiogenic shock? J Card Surg 2012;27: 246–52.

[68] Slottosch I, Liakopoulos O, Kuhn E, Deppe A-C, Scherner M, Madershahian N *et al.* Outcomes after peripheral extracorporeal membrane oxygenation therapy for postcardiotomy cardiogenic shock: a single-center experience. J Surg Res 2013;181:e47–55.

[69] Unosawa S, Sezai A, Hata M, Nakata K, Yoshitake I, Wakui S *et al.* Long-term outcomes of patients undergoing extracorporeal membrane oxygenation for refractory postcardiotomy cardiogenic shock. Surg Today 2013;43:264–70.

[70] Pilarczyk K, Bauer A, Boening A, von der Brelie M, Eichler I, Gohrbandt B *et al.* S3-Guideline: recommendations for intra-aortic balloon pumping in cardiac surgery. Thorac Cardiovasc Surg 2015;63:S131–96.

[71] Chen K, Hou J, Tang H, Hu S. Concurrent implantation of intra-aortic balloon pump and extracorporeal membrane oxygenation improved survival of patients with postcardiotomy shock. Artif Organs 2019;43: 142–9.

[72] Engstrom AE, Granfeldt H, Seybold-Epting W, Dahm M, Cocchieri R, Driessen AH *et al.* Mechanical circulatory support with the Impella 5.0 device for postcardiotomy cardiogenic shock: a three-center experience. Minerva Cardioangiol 2013;61:539–46.

[73] Griffith BP, Anderson MB, Samuels LE, Pae WE Jr, Naka Y, Frazier OH. The RECOVER I: a multicenter prospective study of Impella 5.0/LD for postcardiotomy circulatory support. J Thorac Cardiovasc Surg 2013; 145:548–54.

[74] David CH, Quessard A, Mastroianni C, Hekimian G, Amour J, Leprince P *et al.* Mechanical circulatory support with the Impella 5.0 and the Impella left direct pump for postcardiotomy cardiogenic shock at La Pitié-Salpetriere Hospital. Eur J Cardiothorac Surg 2020;57:183–8.

[75] Thiele H, Sick P, Boudriot E, Diederich KW, Hambrecht R, Niebauer J *et al.* Randomized comparison of intra-aortic balloon support with a percutaneous left ventricular assist device in patients with revascularized acute myocardial infarction complicated by cardiogenic shock. Eur Heart J 2005;26:1276–83.

[76] Hernandez AF, Grab JD, Gammie JS, O'Brien SM, Hammill BG, Rogers JG *et al.* A decade of short-term outcomes in post cardiac surgery ventricular assist device implantation: data from the Society of Thoracic Surgeons' National Cardiac Database. Circulation 2007;116:606–12.

[77] Xiao XJ, Luo ZX, Ye CX, Fan RX, Yi DH, Ji SY *et al.* The short-term pulsatile ventricular assist device for postcardiotomy cardiogenic shock: a clinical trial in China. Artif Organs 2009;33:373–7.

[78] Ando M, Garan AR, Takayama H, Topkara VK, Han J, Kurlansky P *et al.* A continuous-flow external ventricular assist device for cardiogenic shock: evolution over 10 years. J Thorac Cardiovasc Surg 2018;156: 157–65.e1.

[79] Biancari F, Perrotti A, Dalen M, Guerrieri M, Fiore A, Reichart D *et al.* Meta-analysis of the outcome after postcardiotomy venoarterial extracorporeal membrane oxygenation in adult patients. J Cardiothorac Vasc Anesth 2018;32:1175–82.

[80] Biancari F, Dalen M, Perrotti A, Fiore A, Reichart D, Khodabandeh S *et al.* Venoarterial extracorporeal membrane oxygenation after coronary artery bypass grafting: results of a multicenter study. Int J Cardiol 2017;241:109–14.

[81] Loforte A, Marinelli G, Musumeci F, Folesani G, Pilato E, Martin Suarez S *et al.* Extracorporeal membrane oxygenation support in refractory cardiogenic shock: treatment strategies and analysis of risk factors. Artif Organs 2014;38:E129–41.

[82] Beckmann E, Ismail I, Cebotari S, Busse A, Martens A, Shrestha M *et al.* Right-sided heart failure and extracorporeal life support in patients undergoing pericardiectomy for constrictive pericarditis: a risk factor analysis for adverse outcome. Thorac Cardiovasc Surg 2017;65:662–70.

[83] Ko WJ, Lin CY, Chen RJ, Wang SS, Lin FY, Chen YS. Extracorporeal membrane oxygenation support for adult postcardiotomy cardiogenic shock. Ann Thorac Surg 2002;73:538–45.

[84] Zhang R, Kofidis T, Kamiya H, Shrestha M, Tessmann R, Haverich A *et al.* Creatine kinase isoenzyme MB relative index as predictor of mortality on extracorporeal membrane oxygenation support for postcardiotomy cardiogenic shock in adult patients. Eur J Cardiothorac Surg 2006;30:617–20.

[85] Navia JL, Atik FA, Beyer EA, Ruda Vega P. Extracorporeal membrane oxygenation with right axillary artery perfusion. Ann Thorac Surg 2005;79:2163–5.

[86] Biscotti M, Bacchetta M. The "sport model": extracorporeal membrane oxygenation using the subclavian artery. Ann Thorac Surg 2014;98: 1487–9.

[87] Ranney DN, Benrashid E, Meza JM, Keenan JE, Bonadonna DK, Bartz R *et al.* Central cannulation as a viable alternative to peripheral cannulation in extracorporeal membrane oxygenation. Semin Thorac Cardiovasc Surg 2017;29:188–95.

[88] Babu A. Techniques for venoarterial extracorporeal membrane oxygenation support and conversion to temporary left ventricular assist device. Oper Tech Thorac Cardiovasc Surg 2014; 19:365–79.

[89] Juo YY, Skancke M, Sanaiha Y, Mantha A, Jimenez JC, Benharash P. Efficacy of distal perfusion cannulae in preventing limb ischemia during extracorporeal membrane oxygenation: a systematic review and meta-analysis. Artif Organs 2017;41:E263–73.

[90] Calderon D, El-Banayosy A, Koerner MM, Reed AB, Aziz F. Modified T-graft for extracorporeal membrane oxygenation in a patient with small-caliber femoral arteries. Tex Heart Inst J 2015;42:537–9.

[91] Wong JK, Smith TN, Pitcher HT, Hirose H, Cavarocchi NC. Cerebral and lower limb near-infrared spectroscopy in adults on extracorporeal membrane oxygenation. Artif Organs 2012;36:659–67.

[92] Chicotka S, Rosenzweig EB, Brodie D, Bacchetta M. The "Central sport model": extracorporeal membrane oxygenation using the innominate artery for smaller patients as bridge to lung transplantation. ASAIO J 2017;63:e39–44.

[93] Biscotti M, Gannon WD, Agerstrand C, Abrams D, Sonett J, Brodie D *et al.* Awake extracorporeal membrane oxygenation as bridge to lung transplantation: a 9-year experience. Ann Thorac Surg 2017;104: 412–19.

[94] Chamogeorgakis T, Lima B, Shafii AE, Nagpal D, Pokersnik JA, Navia JL *et al.* Outcomes of axillary artery side graft cannulation for extracorporeal membrane oxygenation. J Thorac Cardiovasc Surg 2013;145: 1088–92.

[95] Lorusso R, Raffa MG, Heuts S, Lo Coco V, Meani P, Natour E *et al.* Pulmonary artery cannulation to enhance extracorporeal membrane oxygenation management in acute cardiac failure. Interact CardioVasc Thorac Surg 2019;30:215–22.

[96] Napp LC, Vogel-Claussen J, Schafer A, Haverich A, Bauersachs J, Kuhn C *et al.* First-in-man fully percutaneous complete bypass of heart and lung. JACC Cardiovasc Interv 2017;10:e231–3.

[97] Avalli L, Maggioni E, Sangalli F, Favini G, Formica F, Fumagalli R. Percutaneous left-heart decompression during extracorporeal membrane oxygenation: an alternative to surgical and transeptal venting in adult patients. ASAIO J 2011;57:38–40.

[98] Mitchell IM, Prabhakar G, Maughan J, Taylor DN. Pulmonary artery versus left ventricular venting: a radioisotope study of left ventricular function. Ann Thorac Surg 1989;48:699–703.

Downloaded from https://academic.oup.com/ejcts/article/59/1/12/5918808 by guest on 08 February 2021

[99] Ravichandran AK, Baran DA, Stelling K, Cowger JA, Salerno CT. Outcomes with the Tandem Protek Duo dual-lumen percutaneous right ventricular assist device. ASAIO J 2018;64:570–2.
[100] Avery R, Yu S, Rao P, Wong R, Khalpey Z. Minimally invasive insertion of off-pump central extracorporeal membrane oxygenation. J Card Surg 2017;32:738–40.
[101] Meani P, Delnoij T, Raffa GM, Morici N, Viola G, Sacco A *et al.* Protracted aortic valve closure during peripheral extracorporeal life support: is the intra-aortic balloon pump an effective solution? Perfusion 2019;34:35–41.
[102] Guihaire J, Dang Van S, Rouze S, Rosier S, Roisne A, Langanay T *et al.* Clinical outcomes in patients after extracorporeal membrane oxygenation support for post-cardiotomy cardiogenic shock: a single-centre experience of 92 cases. Interact CardioVasc Thorac Surg 2017; 25:363–9.
[103] 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.
[104] Tepper S, Masood MF, Baltazar Garcia M, Pisani M, Ewald GA, Lasala JM *et al.* Left ventricular unloading by Impella device versus surgical vent during extracorporeal life support. Ann Thorac Surg 2017;104: 861–7.
[105] Lorusso R, Bidar E, Natour E, Heuts S. Minimally invasive management of central extracorporeal membrane oxygenation. J Card Surg 2019; 34:131–3.
[106] 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.
[107] Distelmaier K, Roth C, Schrutka L, Binder C, Steinlechner B, Heinz G *et al.* Beneficial effects of Levosimendan on survival in patients undergoing extracorporeal membrane oxygenation after cardiovascular surgery. Br J Anaesth 2016;117:52–8.
[108] Affronti A, di Bella I, Carino D, Ragni T. Levosimendan may improve weaning outcomes in venoarterial ECMO patients. ASAIO J 2013;59: 554–7.
[109] O'Horo JC, Cawcutt KA, De Moraes AG, Sampathkumar P, Schears GJ. The evidence base for prophylactic antibiotics in patients receiving extracorporeal membrane oxygenation. ASAIO J 2016;62:6–10.
[110] Brogan TLL, Lorusso R, MacLaren G, Peek G. Extracorporeal Life Support: The ELSO Red Book, 1st edn. Ann Arbor, MI, USA: Extracorporeal Life Support Organization, 2017, 832.
[111] Doufle G, Roscoe A, Billia F, Fan E. Echocardiography for adult patients supported with extracorporeal membrane oxygenation. Crit Care 2015;19:326.
[112] Pozzebon S, Blandino Ortiz A, Franchi F, Cristallini S, Belliato M, Lheureux O *et al.* Cerebral near-infrared spectroscopy in adult patients undergoing veno-arterial extracorporeal membrane oxygenation. Neurocrit Care 2018;29:94–104.
[113] Rossello X, Vila M, Rivas-Lasarte M, Ferrero-Gregori A, Sans-Rosello J, Duran-Cambra A *et al.* Impact of pulmonary artery catheter use on short- and long-term mortality in patients with cardiogenic shock. Cardiology 2017;136:61–9.
[114] Sy E, Sklar MC, Lequier L, Fan E, Kanji HD. Anticoagulation practices and the prevalence of major bleeding, thromboembolic events, and mortality in venoarterial extracorporeal membrane oxygenation: a systematic review and meta-analysis. J Crit Care 2017;39:87–96.
[115] Extracorporeal Life Support Organization: Anticoagulation Guideline. https://www.elso.org/portals/0/files/elsoanticoagulationguideline8-2014-table-contents.pdf (10 September 2019, date last accessed).
[116] Guglin M, Zucker MJ, Bazan VM, Bozkurt B, El Banayosy A, Estep JD *et al.* Venoarterial ECMO for adults: JACC scientific expert panel. J Am Coll Cardiol 2019;73:698–716.
[117] Chung YS, Cho DY, Sohn DS, Lee WS, Won H, Lee DH *et al.* Is stopping heparin safe in patients on extracorporeal membrane oxygenation treatment? ASAIO J 2017;63:32–6.
[118] Lo Coco V, Lorusso R, Raffa GM, Malvindi PG, Pilato M, Martucci G *et al.* Clinical complications during veno-arterial extracorporeal membrane oxigenation in post-cardiotomy and non post-cardiotomy shock: still the Achille's heel. J Thorac Dis 2018;10:6993–7004.
[119] Tauber H, Ott H, Streif W, Weigel G, Loacker L, Fritz J *et al.* Extracorporeal membrane oxygenation induces short-term loss of high-molecular-weight von Willebrand factor multimers. Anesth Analg 2015;120:730–6.
[120] Nair P, Hoechter DJ, Buscher H, Venkatesh K, Whittam S, Joseph J *et al.* Prospective observational study of hemostatic alterations during adult extracorporeal membrane oxygenation (ECMO) using point-of-care thromboelastometry and platelet aggregometry. J Cardiothorac Vasc Anesth 2015;29:288–96.
[121] 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.
[122] Extracorporeal Life Support Organization: Guidelines for Adult Cardiac Failure. https://www.elso.org/Portals/0/IGD/Archive/FileManager/e76ef78eabcusersshyerdocumentselsoguidelinesforadultcardiacfailure1.3.pdf (10 September 2019, date last accessed).
[123] Pratt CW, Church FC. Antithrombin: structure and function. Semin Hematol 1991;28:3–9.
[124] Hirsh J, Anand SS, Halperin JL, Fuster V. Mechanism of action and pharmacology of unfractionated heparin. Arterioscler Thromb Vasc Biol 2001;21:1094–6.
[125] Smith A, Hardison D, Bridges B, Pietsch J. Red blood cell transfusion volume and mortality among patients receiving extracorporeal membrane oxygenation. Perfusion 2013;28:54–60.
[126] Koster A, Spiess B, Chew DP, Krabatsch T, Tambeur L, DeAnda A *et al.* Effectiveness of bivalirudin as a replacement for heparin during cardiopulmonary bypass in patients undergoing coronary artery bypass grafting. Am J Cardiol 2004;93:356–9.
[127] Ranucci M, Ballotta A, Kandil H, Isgro G, Carlucci C, Baryshnikova E *et al.*; the Surgical and Clinical Outcome Research Group. Bivalirudin-based versus conventional heparin anticoagulation for postcardiotomy extracorporeal membrane oxygenation. Crit Care 2011;15:R275.
[128] Pieri M, Agracheva N, Bonaveglio E, Greco T, De Bonis M, Covello RD *et al.* Bivalirudin versus heparin as an anticoagulant during extracorporeal membrane oxygenation: a case-control study. J Cardiothorac Vasc Anesth 2013;27:30–4.
[129] Berei TJ, Lillyblad MP, Wilson KJ, Garberich RF, Hryniewicz KM. Evaluation of systemic heparin versus bivalirudin in adult patients supported by extracorporeal membrane oxygenation. ASAIO J 2018;64: 623–9.
[130] Warkentin TE, Greinacher A. Heparin-induced thrombocytopaenia and cardiac surgery. Ann Thorac Surg 2003;76:2121–31.
[131] Glick D, Dzierba AL, Abrams D, Muir J, Eisenberger A, Diuguid D *et al.* Clinically suspected heparin-induced thrombocytopaenia during extracorporeal membrane oxygenation. J Crit Care 2015;30:1190–4.
[132] Bembea MM, Annich G, Rycus P, Oldenburg G, Berkowitz I, Pronovost P. Variability in anticoagulation management of patients on extracorporeal membrane oxygenation: an international survey. Pediatr Crit Care Med 2013;14:e77–84.
[133] Atallah S, Liebl M, Fitousis K, Bostan F, Masud F. Evaluation of the activated clotting time and activated partial thromboplastin time for the monitoring of heparin in adult extracorporeal membrane oxygenation patients. Perfusion 2014;29:456–61.
[134] Warkentin TE, Heddle NM. Laboratory diagnosis of immune heparin-induced thrombocytopaenia. Curr Hematol Rep 2003;2:148–57.
[135] Haft JW. Temporary mechanical circulatory support for postcardiotomy shock: don't come late to the party. J Thorac Cardiovasc Surg 2015;149:1451–2.
[136] van Diepen S, Katz JN, Albert NM, Henry TD, Jacobs AK, Kapur NK *et al.* Contemporary management of cardiogenic shock: a scientific statement From the American Heart Association. Circulation 2017;136: e232–68.
[137] Koeckert MS, Jorde UP, Naka Y, Moses JW, Takayama H. Impella LP 2.5 for left ventricular unloading during venoarterial extracorporeal membrane oxygenation support. J Card Surg 2011;26:666–8.
[138] Myburgh JA, Mythen MG. Resuscitation fluids. N Engl J Med 2013;369: 1243–51.
[139] Fullerton DA, McIntyre RC Jr, Kirson LE, St Cyr JA, Whitman GJ, Grover FL. Impact of respiratory acid-base status in patients with pulmonary hypertension. Ann Thorac Surg 1996;61:696–701.
[140] Maldonado Y, Singh S, Taylor MA. Cerebral near-infrared spectroscopy in perioperative management of left ventricular assist device and extracorporeal membrane oxygenation patients. Curr Opin Anaesthesiol 2014;27:81–8.
[141] Jansen TC, van Bommel J, Schoonderbeek FJ, Sleeswijk Visser SJ, van der Klooster JM, Lima AP *et al.* Early lactate-guided therapy in intensive care unit patients: a multicenter, open-label, randomized controlled trial. Am J Respir Crit Care Med 2010;182:752–61.

Downloaded from https://academic.oup.com/ejcts/article/59/1/12/5918808 by guest on 08 February 2021

[142] Vincent J-L, De Backer D. Circulatory Shock. N Engl J Med 2013;369: 1726–34.
[143] Petersen JW, Felker GM. Inotropes in the management of acute heart failure. Crit Care Med 2008;36:S106–11.
[144] Roussel A, Al-Attar N, Alkhoder S, Radu C, Raffoul R, Alshammari M *et al.* Outcomes of percutaneous femoral cannulation for venoarterial extracorporeal membrane oxygenation support. Eur Heart J Acute Cardiovasc Care 2012;1:111–14.
[145] Vallabhajosyula P, Kramer M, Lazar S, McCarthy F, Rame E, Wald J *et al.* Lower-extremity complications with femoral extracorporeal life support. J Thorac Cardiovasc Surg 2016;151:1738–44.
[146] Lamb KM, DiMuzio PJ, Johnson A, Batista P, Moudgill N, McCullough M *et al.* Arterial protocol including prophylactic distal perfusion catheter decreases limb ischemia complications in patients undergoing extracorporeal membrane oxygenation. J Vasc Surg 2017;65:1074–9.
[147] Patton-Rivera K, Beck J, Fung K, Chan C, Beck M, Takayama H *et al.* Using near-infrared reflectance spectroscopy (NIRS) to assess distal-limb perfusion on venoarterial (V-A) extracorporeal membrane oxygenation (ECMO) patients with femoral cannulation. Perfusion 2018;33:618–23.
[148] Stephens RS, Shah AS, Whitman GJ. Lung injury and acute respiratory distress syndrome after cardiac surgery. Ann Thorac Surg 2013;95: 1122–9.
[149] Ahmed AH, Litell JM, Malinchoc M, Kashyap R, Schiller HJ, Pannu SR *et al.* The role of potentially preventable hospital exposures in the development of acute respiratory distress syndrome: a population-based study. Crit Care Med 2014;42:31–9.
[150] Jenks CL, Tweed J, Gigli KH, Venkataraman R, Raman L. An international survey on ventilator practices among extracorporeal membrane oxygenation centers. ASAIO J 2017;63:787–92.
[151] Rubino A, Costanzo D, Stanszus D, Valchanov K, Jenkins D, Sertic F *et al.* Central veno-arterial extracorporeal membrane oxygenation (C-VA-ECMO) after cardiothoracic surgery: a single-center experience. J Cardiothorac Vasc Anesth 2018;32:1169–74.
[152] Toeg H, French D, Gilbert S, Rubens F. Incidence of sternal wound infection after tracheostomy in patients undergoing cardiac surgery: a systematic review and meta-analysis. J Thorac Cardiovasc Surg 2017; 153:1394–400.e7.
[153] Fagon JY. Diagnosis and treatment of ventilator-associated pneumonia: fiberoptic bronchoscopy with bronchoalveolar lavage is essential. Semin Respir Crit Care Med 2006;27:34–44.
[154] Schmidt M, Brechot N, Hariri S, Guiguet M, Luyt CE, Makri R *et al.* Nosocomial infections in adult cardiogenic shock patients supported by venoarterial extracorporeal membrane oxygenation. Clin Infect Dis 2012;55:1633–41.
[155] Bouadma L, Mourvillier B, Deiler V, Le Corre B, Lolom I, Regnier B *et al.* A multifaceted program to prevent ventilator-associated pneumonia: impact on compliance with preventive measures. Crit Care Med 2010;38:789–96.
[156] Biffi S, Di Bella S, Scaravilli V, Peri AM, Grasselli G, Alagna L *et al.* Infections during extracorporeal membrane oxygenation: epidemiology, risk factors, pathogenesis and prevention. Int J Antimicrob Agents 2017;50:9–16.
[157] Rupprecht L, Lunz D, Philipp A, Lubnow M, Schmid C. Pitfalls in percutaneous ECMO cannulation. Heart Lung Vessel 2015;7:320–6.
[158] Brown KL, Ridout DA, Shaw M, Dodkins I, Smith LC, O'Callaghan Ma *et al.* Healthcare-associated infection in pediatric patients on extracorporeal life support: the role of multidisciplinary surveillance. Pediatr Crit Care Med 2006;7:546–50.
[159] Glater-Welt LB, Schneider JB, Zinger MM, Rosen L, Sweberg TM. Nosocomial bloodstream infections in patients receiving extracorporeal life support: variability in prevention, practices: a survey of the Extracorporeal Life Support Organization. J Intensive Care Med 2016; 31:654–9.
[160] O'Horo JC, Silva GL, Munoz-Price LS, Safdar N. The efficacy of daily bathing with chlorhexidine for reducing healthcare-associated bloodstream infections: a meta-analysis. Infect Control Hosp Epidemiol 2012;33:257–67.
[161] Gaynes R. The impact of antimicrobial use on the emergence of antimicrobial-resistant bacteria in hospitals. Infect Dis Clin North Am 1997;11:757–65.
[162] Rhodes A, Evans LE, Alhazzani W, Levy MM, Antonelli M, Ferrer R *et al.* Surviving sepsis campaign: international guidelines for management of sepsis and septic shock: 2016. Intensive Care Med 2017;43: 304–77.
[163] Wang Y, Bellomo R. Cardiac surgery-associated acute kidney injury: risk factors, pathophysiology and treatment. Nat Rev Nephrol 2017;13: 697–711.
[164] Lin CY, Chen YC, Tsai FC, Tian YC, Jenq CC, Fang JT *et al.* RIFLE classification is predictive of short-term prognosis in critically ill patients with acute renal failure supported by extracorporeal membrane oxygenation. Nephrol Dial Transplant 2006;21:2867–73.
[165] Chen H, Yu RG, Yin NN, Zhou JX. Combination of extracorporeal membrane oxygenation and continuous renal replacement therapy in critically ill patients: a systematic review. Crit Care 2014;18:675.
[166] Ha MA, Sieg AC. Evaluation of altered drug pharmacokinetics in critically ill adults receiving extracorporeal membrane oxygenation. Pharmacotherapy 2017;37:221–35.
[167] Schetz M. Drug dosing in continuous renal replacement therapy: general rules. Curr Opin Crit Care 2007;13:645–51.
[168] Suga N, Matsumura Y, Abe R, Hattori N, Nakada TA, Oda S. A safe procedure for connecting a continuous renal replacement therapy device into an extracorporeal membrane oxygenation circuit. J Artif Organs 2017;20:125–31.
[169] Lorusso R, Barili F, Mauro MD, Gelsomino S, Parise O, Rycus PT *et al.* In-hospital neurologic complications in adult patients undergoing venoarterial extracorporeal membrane oxygenation: results from the Extracorporeal Life Support Organization registry. Crit Care Med 2016; 44:e964–72.
[170] Cho S-M, Farrokh S, Whitman G, Bleck TP, Geocadin RG. Neurocritical care for ECMO patients. Crit Care Med 2019;47:1773–81.
[171] Cho SM, Choi CW, Whitman G, Suarez JI, Martinez NC, Geocadin RG *et al.* Neuropsychological findings and brain injury pattern in patients on ECMO. Clin EEG Neurosci 2019; doi:10.1177/1550059419892757.
[172] Sinnah F, Dalloz M-A, Magalhaes E, Wanono R, Neuville M, Smonig R *et al.* Early electroencephalography findings in cardiogenic shock patients treated by venoarterial extracorporeal membrane oxygenation. Crit Care Med 2018;46:e389–94.
[173] Cho SM, Ziai W, Mayasi Y, Gusdon AM, Creed J, Sharrock M *et al.* Noninvasive neurological monitoring in extracorporeal membrane oxygenation. ASAIO J 2020;66:388–93.
[174] Aissaoui N, El-Banayosy A, Combes A. How to wean a patient from veno-arterial extracorporeal membrane oxygenation. Intensive Care Med 2015;41:902–5.
[175] Cavarocchi NC, Pitcher HT, Yang Q, Karbowski P, Miessau J, Hastings HM *et al.* Weaning of extracorporeal membrane oxygenation using continuous hemodynamic transesophageal echocardiography. J Thorac Cardiovasc Surg 2013;146:1474–9.
[176] Kurihara C, Kawabori M, Sugiura T, Critsinelis AC, Wang S, Cohn WE *et al.* Bridging to a long-term ventricular assist device with short-term mechanical circulatory support. Artif Organs 2018;42:589–96.
[177] Tsyganenko D, Gromann TW, Schoenrath F, Mueller M, Mulzer J, Starck C *et al.* Predictors of mid-term outcomes in patients undergoing implantation of a ventricular assist device directly after extracorporeal life support. Eur J Cardiothorac Surg 2019;55:773–9.
[178] Bermudez CA, McMullan DM. Extracorporeal life support in preoperative and postoperative heart transplant management. Ann Transl Med 2017;5:398.
[179] Davies RR, Russo MJ, Hong KN, O'Byrne ML, Cork DP, Moskowitz AJ *et al.* The use of mechanical circulatory support as a bridge to transplantation in pediatric patients: an analysis of the United Network for Organ Sharing database. J Thorac Cardiovasc Surg 2008;135:421–7, 7.e1.
[180] Fukuhara S, Takeda K, Kurlansky PA, Naka Y, Takayama H. Extracorporeal membrane oxygenation as a direct bridge to heart transplantation in adults. J Thorac Cardiovasc Surg 2018;155:1607–18.e6.
[181] Chen SW, Tsai FC, Lin YS, Chang CH, Chen DY, Chou AH *et al.* Long-term outcomes of extracorporeal membrane oxygenation support for postcardiotomy shock. J Thorac Cardiovasc Surg 2017;154:469–77.e2.
[182] Roth C, Schrutka L, Binder C, Kriechbaumer L, Heinz G, Lang IM *et al.* Liver function predicts survival in patients undergoing extracorporeal membrane oxygenation following cardiovascular surgery. Crit Care 2016;20:57.
[183] Distelmaier K, Roth C, Binder C, Schrutka L, Schreiber C, Hoffelner F *et al.* Urinary output predicts survival in patients undergoing extracorporeal membrane oxygenation following cardiovascular surgery. Crit Care Med 2016;44:531–8.
[184] Narotsky DL, Mosca MS, Mochari-Greenberger H, Beck J, Liao M, Mongero L *et al.* Short-term and longer-term survival after veno-

Downloaded from https://academic.oup.com/ejcts/article/59/1/12/5918808 by guest on 08 February 2021

arterial extracorporeal membrane oxygenation in an adult patient population: does older age matter? Perfusion 2016;31:366–75.
[185] Meani P, Matteucci M, Jiritano F, Fina D, Panzeri F, Raffa GM et al. Long-term survival and major outcomes in post-cardiotomy extracorporeal membrane oxygenation for adult patients in cardiogenic shock. Ann Cardiothorac Surg 2019;8:116–22.
[186] Khorsandi M, Shaikhrezai K, Prasad S, Pessotto R, Walker W, Berg G et al. Advanced mechanical circulatory support for post-cardiotomy cardiogenic shock: a 20-year outcome analysis in a non-transplant unit. J Cardiothorac Surg 2016;11:29.
[187] Lewis AR, Wray J, O'Callaghan M, Wroe AL. Parental symptoms of posttraumatic stress after pediatric extracorporeal membrane oxygenation. Pediatr Crit Care Med 2014;15:e80–8.
[188] Harris-Fox S. The experience of being an 'extracorporeal membrane oxygenation' relative within the CESAR trial. Nurs Crit Care 2012;17: 9–18.
[189] Bein T, Brodie D. Understanding ethical decisions for patients on extracorporeal life support. Intensive Care Med 2017;43:1510–11.
[190] Mavroudis C, Mavroudis CD, Green J, Sade RM, Jacobs JP, Kodish E. Ethical considerations for post-cardiotomy extracorporeal membrane oxygenation. Cardiol Young 2012;22:780–6.
[191] Stephens AL, Bruce CR. Setting expectations for ECMO: improving communication between clinical teams and decision makers. Methodist Debakey Cardiovasc J 2018;14:120–5.
[192] Abrams DC, Prager K, Blinderman CD, Burkart KM, Brodie D. Ethical dilemmas encountered with the use of extracorporeal membrane oxygenation in adults. Chest 2014;145:876–82.
[193] Meltzer EC, Ivascu NS, Stark M, Orfanos AV, Acres CA, Christos PJ et al. A survey of physicians' attitudes toward decision-making authority for initiating and withdrawing VA-ECMO: results and ethical implications for shared decision making. J Clin Ethics 2016;27:281–9.
[194] Doorenbos AZ, Starks H, Bourget E, McMullan DM, Lewis-Newby M, Rue TC et al. Examining palliative care team involvement in automatic consultations for children on extracorporeal life support in the pediatric intensive care unit. J Palliat Med 2013;16:492–5.
[195] Fann JI, Calhoon JH, Carpenter AJ, Merrill WH, Brown JW, Poston RS et al. Simulation in coronary artery anastomosis early in cardiothoracic surgical residency training: the Boot Camp experience. J Thorac Cardiovasc Surg 2010;139:1275–81.
[196] Brogan T. ECMO Specialist Training Manual, 4th edn. Ann Arbor, MI, USA: Extracorporeal Life Support Organization, 2018.
[197] Lorello GR, Cook DA, Johnson RL, Brydges R. Simulation-based training in anaesthesiology: a systematic review and meta-analysis. Br J Anaesth 2014;112:231–45.
[198] Chan SY, Figueroa M, Spentzas T, Powell A, Holloway R, Shah S. Prospective assessment of novice learners in a simulation-based extracorporeal membrane oxygenation (ECMO) education program. Pediatr Cardiol 2013;34:543–52.
[199] Zakhary BM, Kam LM, Kaufman BS, Felner KJ. The utility of high-fidelity simulation for training critical care fellows in the management of extracorporeal membrane oxygenation emergencies: a randomized controlled trial. Crit Care Med 2017;45:1367–73.
[200] Anderson JM, Murphy AA, Boyle KB, Yaeger KA, Halamek LP. Simulating extracorporeal membrane oxygenation emergencies to improve human performance. Part II: assessment of technical and behavioral skills. Simul Healthc 2006;1:228–32.
[201] Anderson JM, Boyle KB, Murphy AA, Yaeger KA, LeFlore J, Halamek LP. Simulating extracorporeal membrane oxygenation emergencies to improve human performance. Part I: methodologic and technologic innovations. Simul Healthc 2006;1:220–7.
[202] Burkhart HM, Riley JB, Lynch JJ, Suri RM, Greason KL, Joyce LD et al. Simulation-based postcardiotomy extracorporeal membrane oxygenation crisis training for thoracic surgery residents. Ann Thorac Surg 2013;95:901–6.
[203] Nallamothu BK, Eagle KA, Ferraris VA, Sade RM. Should coronary artery bypass grafting be regionalized? Ann Thorac Surg 2005;80: 1572–81.
[204] Barbaro RP, Odetola FO, Kidwell KM, Paden ML, Bartlett RH, Davis MM et al. Association of hospital-level volume of extracorporeal membrane oxygenation cases and mortality. Analysis of the Extracorporeal Life Support Organization registry. Am J Respir Crit Care Med 2015;191:894–901.
[205] Ranney DN, Bonadonna D, Yerokun BA, Mulvihill MS, Al-Rawas N, Weykamp M et al. Extracorporeal membrane oxygenation and interfacility transfer: a regional referral experience. Ann Thorac Surg 2017; 104:1471–8.
[206] Salna M, Chicotka S, Biscotti M, Agerstrand C, Liou P, Ginsburg M et al. Management of surge in extracorporeal membrane oxygenation transport. Ann Thorac Surg 2018;105:528–34.
[207] Extracorporeal Life Support Organization: Guidelines for ECMO Transport. https://www.elso.org/Portals/0/Files/ELSO%20GUIDELINES%20FOR%20ECMO%20TRANSPORT_May2015.pdf (10 September 2019, date last accessed).
[208] Odell RM, Erickson R, McEwan RM. Identification and certification of extracorporeal membrane oxygenation specialists in the United States. ASAIO J 1992;38:858–61.
[209] Searles B, Gunst G, Terry B, Melchior R, Darling E. 2004 survey of ECMO in the neonate after open heart surgery: circuitry and team roles. J Extra Corpor Technol 2005;37:351–4.
[210] Guillo Moreno V, Gutierrez Martinez A, Romero Berrocal A, Sanchez Castilla M, Garcia-Fernandez J. Experience in the management of ECMO therapy as a mortality risk factor Experiencia en el manejo de terapia ECMO como factor de riesgo de mortalidad. Rev Esp Anestesiol Reanim 2018;65:90–5.
[211] Na SJ, Chung CR, Choi HJ, Cho YH, Sung K, Yang JH et al. The effect of multidisciplinary extracorporeal membrane oxygenation team on clinical outcomes in patients with severe acute respiratory failure. Ann Intensive Care 2018;8:31.
[212] Leape LL, Cullen DJ, Clapp MD, Burdick E, Demonaco HJ, Erickson JI et al. Pharmacist participation on physician rounds and adverse drug events in the intensive care unit. JAMA 1999; 282:267–70.
[213] Dowding D, Randell R, Gardner P, Fitzpatrick G, Dykes P, Favela J et al. Dashboards for improving patient care: review of the literature. Int J Med Inform 2015;84:87–100.
[214] Garland A. Improving quality of care in ICUs. Intensive Crit Care Med 2009;81–91; doi:10.1007/978-88-470-1436-7_8.
[215] Dalia AA, Ortoleva J, Fiedler A, Villavicencio M, Shelton K, Cudemus GD. Extracorporeal membrane oxygenation is a team sport: institutional survival benefits of a formalized ECMO team. J Cardiothorac Vasc Anesth 2019;33:902–7.
[216] Kim MM, Barnato AE, Angus DC, Fleisher LA, Kahn JM. The effect of multidisciplinary care teams on intensive care unit mortality. Arch Intern Med 2010;170:369–76.
[217] Na SJ, Park TK, Lee GY, Cho YH, Chung CR, Jeon K et al. Impact of a cardiac intensivist on mortality in patients with cardiogenic shock. Int J Cardiol 2017;244:220–5.
[218] Pronovost PJ, Jenckes MW, Dorman T, Garrett E, Breslow MJ, Rosenfeld BA et al. Organizational characteristics of intensive care units related to outcomes of abdominal aortic surgery. JAMA 1999; 281:1310–17.
[219] LaPar DJ, Ghanta RK, Kern JA, Crosby IK, Rich JB, Speir AM et al. Hospital variation in mortality from cardiac arrest after cardiac surgery: an opportunity for improvement? Ann Thorac Surg 2014;98: 534–9.
[220] Robert WN, Michael S, Clifton WC, Lana MG, Dianne LA, Farhan B et al. Part 1: executive Summary. Circulation 2015;132:S315–67.
[221] Richardson AS, Schmidt M, Bailey M, Pellegrino VA, Rycus PT, Pilcher DV. ECMO cardio-pulmonary resuscitation (ECPR), trends in survival from an international multicentre cohort study over 12-years. Resuscitation 2017;112:34–40.
[222] Kaushal M, Schwartz J, Gupta N, Im J, Leff J, Jakobleff WA et al. Patient demographics and extracorporeal membranous oxygenation (ECMO)-related complications associated with survival to discharge or 30-day survival in adult patients receiving venoarterial (VA) and venovenous (VV) ECMO in a quaternary care urban center. J Cardiothorac Vasc Anesth 2019;33:910–17.
[223] Pozzi M, Armoiry X, Achana F, Koffel C, Pavlakovic I, Lavigne F et al. Extracorporeal life support for refractory cardiac arrest: a 10-year comparative analysis. Ann Thorac Surg 2019;107:809–16.
[224] Extracorporeal Life Support Organization: Guidelines for ECPR Cases. https://www.elso.org/Portals/0/IGD/Archive/FileManager/6713186745cusersshyerdocumentselsoguidelinesforecprcases1.3.pdf (10 September 2019, date last accessed).
[225] Michels G, Wengenmayer T, Hagl C, Dohmen C, Bottiger BW, Bauersachs J et al. Recommendations for extracorporeal cardiopulmonary resuscitation (ECPR): consensus statement of DGIIN, DGK, DGTHG, DGfK, DGNI, DGAI, DIVI and GRC. Clin Res Cardiol 2019;108: 455–64.
[226] Park BS, Lee WY, Lim JH, Ra YJ, Kim YH, Kim HS. Delayed repair of ventricular septal rupture following preoperative awake extracorporeal

Downloaded from https://academic.oup.com/ejcts/article/59/1/112/5918808 by guest on 08 February 2021

membrane oxygenation support. Korean J Thorac Cardiovasc Surg 2017;50:211–14.
[227] McLaughlin A, McGiffin D, Winearls J, Tesar P, Cole C, Vallely M *et al*. Veno-arterial ECMO in the setting of post-infarct ventricular septal defect: a bridge to surgical repair. Heart Lung Circ 2016;25:1063–6.
[228] Kim TS, Na CY, Baek JH, Kim JH, Oh SS. Preoperative extracorporeal membrane oxygenation for severe ischemic mitral regurgitation—2 case reports. Korean J Thorac Cardiovasc Surg 2011;44:236–9.
[229] Dobrilovic N, Lateef O, Michalak L, Delibasic M, Raman J. Extracorporeal membrane oxygenation bridges inoperable patients to definitive cardiac operation. ASAIO J 2019;65:43–8.
[230] Tseng PH, Wang SS, Shih FJ. Changes in health-related quality of life across three post-heart transplantation stages: preoperative extracorporeal membrane versus non-extracorporeal membrane group/clinical trial plan group versus non-clinical trial plan group in Taiwan. Transplant Proc 2012;44:915–18.
[231] Lorusso R, Gelsomino S, Carella R, Livi U, Mariscalco G, Onorati F *et al.* Impact of prophylactic intra-aortic balloon counter-pulsation on postoperative outcome in high-risk cardiac surgery patients: a multicentre, propensity-score analysis. Eur J Cardiothorac Surg 2010;38:585–91.
[232] Jaidka A, De S, Nagpal DA, Chu M. Prophylactic right ventricular assist device for high-risk patients undergoing valve corrective surgery. Can J Circ 2019;1:19–27.
[233] Rubenfeld GD, Caldwell E, Peabody E, Weaver J, Martin DP, Neff M *et al.* Incidence and outcomes of acute lung injury. N Engl J Med 2005; 353:1685–93.
[234] Rong LQ, Di Franco A, Gaudino M. Acute respiratory distress syndrome after cardiac surgery. J Thorac Dis 2016;8:E1177–86.
[235] Weissman C. Pulmonary complications after cardiac surgery. Semin Cardiothorac Vasc Anesth 2004;8:185–211.
[236] Peek GJ, Clemens F, Elbourne D, Firmin R, Hardy P, Hibbert C *et al.* CESAR: conventional ventilatory support vs extracorporeal membrane oxygenation for severe adult respiratory failure. BMC Health Serv Res 2006;6:163.
[237] Song JH, Woo WK, Song SH, Kim HH, Kim BJ, Kim HE *et al.* Outcome of veno-venous extracorporeal membrane oxygenation use in acute respiratory distress syndrome after cardiac surgery with cardiopulmonary bypass. J Thorac Dis 2016;8:1804–13.
[238] Seo DJ, Yoo JS, Kim JB, Jung SH, Choo SJ, Chung CH *et al.* Venovenous extracorporeal membrane oxygenation for postoperative acute respiratory distress syndrome. Korean J Thorac Cardiovasc Surg 2015;48:180–6.
[239] Lund LH, Edwards LB, Kucheryavaya AY, Benden C, Dipchand AI, Goldfarb S *et al.* The registry of the International Society for Heart and Lung Transplantation: thirty-second official adult heart transplantation report—2015; focus theme: early graft failure. J Heart Lung Transplant 2015;34:1244–54.
[240] Kobashigawa J, Zuckermann A, Macdonald P, Leprince P, Esmailian F, Luu M *et al.* Report from a consensus conference on primary graft dysfunction after cardiac transplantation. J Heart Lung Transplant 2014;33:327–40.
[241] Tanaka D, Hirose H, Cavarocchi N, Entwistle JW. The impact of vascular complications on survival of patients on venoarterial extracorporeal membrane oxygenation. Ann Thorac Surg 2016;101:1729–34.
[242] Williams B, Bernstein W. Review of venoarterial extracorporeal membrane oxygenation and development of intracardiac thrombosis in adult cardiothoracic patients. J Extra Corpor Technol 2016;48:162–7.
[243] D'Alessandro C, Aubert S, Golmard JL, Praschker BL, Luyt CE, Pavie A *et al.* Extra-corporeal membrane oxygenation temporary support for early graft failure after cardiac transplantation. Eur J Cardiothorac Surg 2010;37:343–9.
[244] 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.
[245] Tran BG, De La Cruz K, Grant S, Meltzer J, Benharash P, Dave R *et al.* Temporary venoarterial extracorporeal membrane oxygenation: ten-year experience at a cardiac transplant center. J Intensive Care Med 2018;33:288–95.
[246] Patlolla B, Beygui R, Haddad F. Right-ventricular failure following left ventricle assist device implantation. Curr Opin Cardiol 2013;28: 223–33.
[247] Deng MC, Edwards LB, Hertz MI, Rowe AW, Keck BM, Kormos R *et al.* Mechanical circulatory support device database of the International Society for Heart and Lung Transplantation: third annual report–2005. J Heart Lung Transplant 2005;24:1182–7.
[248] Fischer Q, Kirsch M. Liberal right ventricular assist device extracorporeal membrane oxygenation support for right ventricular failure after implantable left ventricular assist device placement. ASAIO J 2018;64: 741–7.
[249] Mohite PN, Sabashnikov A, De Robertis F, Popov AF, Simon AR. Oxy-RVAD: rescue in pulmonary complications after LVAD implantation. Perfusion 2015;30:596–9.

Downloaded from https://academic.oup.com/ejcts/article/59/1/12/5918808 by guest on 08 February 2021