


# Use of extracorporeal circulation (ECLS/ECMO) for cardiac and circulatory failure –A clinical practice Guideline Level 3

Alexander Assmann<sup>1\*†</sup> , Andreas Beckmann<sup>2†</sup>, Christof Schmid<sup>3</sup>, Karl Werdan<sup>4</sup>, Guido Michels<sup>5</sup>, Oliver Miera<sup>6</sup>, Florian Schmidt<sup>7</sup>, Stefan Klotz<sup>8</sup>, Christoph Starck<sup>9</sup>, Kevin Pilarczyk<sup>10</sup>, Ardawan Rastan<sup>11</sup>, Marion Burckhardt<sup>12</sup>, Monika Nothacker<sup>13</sup>, Ralf Muellenbach<sup>14</sup>, York Zausig<sup>15</sup>, Nils Haake<sup>10</sup>, Heinrich Groesdonk<sup>16</sup>, Markus Ferrari<sup>17</sup>, Michael Buerke<sup>18</sup>, Marcus Hennersdorf<sup>19</sup>, Mark Rosenberg<sup>20</sup>, Thomas Schaible<sup>21</sup>, Harald Köditz<sup>22</sup>, Stefan Kluge<sup>23</sup>, Uwe Janssens<sup>24</sup>, Matthias Lubnow<sup>25</sup>, Andreas Flemmer<sup>26</sup>, Susanne Herber-Jonat<sup>27</sup>, Lucas Wessel<sup>28</sup>, Dirk Buchwald<sup>29</sup>, Sven Maier<sup>30</sup>, Lars Krüger<sup>31</sup>, Andreas Fründ<sup>32</sup>, Rolf Jaksties<sup>33</sup>, Stefan Fischer<sup>34</sup>, Karsten Wiebe<sup>35</sup>, Christiane S. Hartog<sup>36</sup>, Omer Dzemali<sup>37</sup>, Daniel Zimpfer<sup>38</sup>, Elfriede Ruttman-Ulmer<sup>39</sup>, Christian Schlensak<sup>40</sup>, Malte Kelm<sup>41</sup>, Stephan Ensminger<sup>42</sup> and Udo Boeken<sup>1</sup>

<sup>1</sup>Department of Cardiac Surgery, Heinrich Heine University, Medical Faculty, Moorenstr. 5, Düsseldorf, 40225, Germany; <sup>2</sup>German Society for Thoracic and Cardiovascular Surgery, Langenbeck-Virchow-Haus, Berlin, Germany; <sup>3</sup>Department of Cardiothoracic Surgery, University Medical Center Regensburg, Regensburg, Germany; <sup>4</sup>Clinic for Internal Medicine III, University Hospital Halle (Saale), Martin-Luther University Halle-Wittenberg, Halle, Germany; <sup>5</sup>Department of Acute and Emergency Care, St Antonius Hospital Eschweiler, Eschweiler, Germany; <sup>6</sup>Department of Congenital Heart Disease-Pediatric Cardiology, German Heart Center Berlin, Berlin, Germany; <sup>7</sup>Department of Pediatric Cardiology and Intensive Care Medicine, Medical School Hannover, Hannover, Germany; <sup>8</sup>Department of Cardiac Surgery, Segeberger Kliniken, Bad Segeberg, Germany; <sup>9</sup>Department of Cardiothoracic and Vascular Surgery, German Heart Centre, Berlin, Germany; <sup>10</sup>Department for Intensive Care Medicine, Imland Hospital Rendsburg, Rendsburg, Schleswig-Holstein, Germany; <sup>11</sup>Department of Cardiac and Vascular Thoracic Surgery, Philipps-University Hospital Marburg, Marburg, Germany; <sup>12</sup>Department of Health Sciences and Management, Baden-Wuerttemberg Cooperative State University (DHBW), Stuttgart, Germany; <sup>13</sup>Institute for Medical Knowledge Management, Association of the Scientific Medical Societies (AWMF), Universität Marburg, Marburg, Germany; <sup>14</sup>Department of Anaesthesiology and Critical Care Medicine, Campus Kassel of the University of Southampton, Kassel, Germany; <sup>15</sup>Department of Anesthesiology and Operative Intensive Care Medicine, Aschaffenburg-Alzenau Hospital, Aschaffenburg, Bavaria, Germany; <sup>16</sup>Department of Intensive Care Medicine, Helios Clinic Erfurt, Erfurt, Germany; <sup>17</sup>HSK, Clinic of Internal Medicine I, Helios-Kliniken, Wiesbaden, Germany; <sup>18</sup>Department of Cardiology, Angiology and Internal Intensive Care Medicine, St. Marienkrankenhaus Siegen, Siegen, Germany; <sup>19</sup>Department of Cardiology, Pneumology, Angiology and Internal Intensive Care Medicine, SLK-Kliniken Heilbronn, Heilbronn, Germany; <sup>20</sup>Klinikum Aschaffenburg-Alzenau, Medizinische Klinik I, Aschaffenburg, Germany; <sup>21</sup>Department of Neonatology, University Children's Hospital Mannheim, University of Heidelberg, Mannheim, Germany; <sup>22</sup>Medical University Children's Hospital, Hannover, Germany; <sup>23</sup>Klinik für Intensivmedizin, Universitätsklinikum Hamburg-Eppendorf, Hamburg, Germany; <sup>24</sup>Medical Clinic and Medical Intensive Care Medicine, St Antonius Hospital, Eschweiler, Germany; <sup>25</sup>Department of Internal Medicine II, University Hospital Regensburg, Regensburg, Germany; <sup>26</sup>Division of Neonatology, Dr. v. Hauner Children's Hospital and Perinatal Center Munich - Grosshadern, LMU Munich, Munich, Germany; <sup>27</sup>Division of Neonatology, Dr. v. Hauner Children's Hospital and Perinatal Center Munich - Grosshadern, LMU Munich, Munich, Germany; <sup>28</sup>Department of Pediatric Surgery, Medical Faculty Mannheim, University of Heidelberg, Heidelberg, Germany; <sup>29</sup>Department of Cardiothoracic Surgery, University Hospital Bergmannsheil, Ruhr-University, Bochum, Germany; <sup>30</sup>Department of Cardiovascular Surgery, Heart Center Freiburg University, Freiburg, Germany; <sup>31</sup>Division of Thoracic and Cardiovascular Surgery, Heart- and Diabetescentre NRW, Ruhr-University, Bochum, Germany; <sup>32</sup>Department of Physiotherapy, Heart- and Diabetescentre NRW, Ruhr-University, Bochum, Germany; <sup>33</sup>German Heart Foundation, Germany; <sup>34</sup>Department of Thoracic Surgery and Lung Support, Ibbenbueren General Hospital, Ibbenbueren, Germany; <sup>35</sup>Department of Cardiothoracic Surgery, Münster University Hospital, Münster, Germany; <sup>36</sup>Department of Anesthesiology and Operative Intensive Care Medicine, Charité Universitätsmedizin Berlin, and Klinik Bavaria, Kreischa, Germany; <sup>37</sup>Department of Cardiac Surgery, Triemli City Hospital Zurich, Zurich, Switzerland; <sup>38</sup>Department of Cardiac Surgery, Medical University of Vienna, Vienna, Austria; <sup>39</sup>Department of Cardiac Surgery, Medical University of Innsbruck, Innsbruck, Austria; <sup>40</sup>Department of Cardio-Thoracic and Vascular Surgery, University of Tübingen, Tübingen, Germany; <sup>41</sup>Department of Cardiology, Pulmonology and Vascular Medicine, Heinrich Heine University, Medical Faculty, Düsseldorf, Germany; and <sup>42</sup>Department of Cardiac and Thoracic Vascular Surgery, University Hospital of Schleswig-Holstein, Lübeck, Germany

## Abstract

**Aims** Worldwide applications of extracorporeal circulation for mechanical support in cardiac and circulatory failure, which are referred to as extracorporeal life support (ECLS) or veno-arterial extracorporeal membrane oxygenation (va-ECMO), have dramatically increased over the past decade. In spite of the expanding use and the immense medical as well as socio-economic impact of this therapeutic approach, there has been a lack of interdisciplinary recommendations considering the best available evidence for ECLS treatment.

**Methods and Results** In a multiprofessional, interdisciplinary scientific effort of all scientific societies involved in the treatment of patients with acute cardiac and circulatory failure, the first evidence- and expert consensus-based guideline (level S3) on ECLS/ECMO therapy was developed in a structured approach under regulations of the AWMF (Association of the Scientific Medical Societies in Germany) and under use of GRADE (Grading of Recommendations Assessment, Development and

Evaluation) criteria. This article presents all recommendations created by the expert panel, addressing a multitude of aspects for ECLS initiation, continuation, weaning and aftercare as well as structural and personnel requirements.

**Conclusions** This first evidence- and expert consensus-based guideline (level S3) on ECLS/ECMO therapy should be used to apply the best available care nationwide. Beyond clinical practice advice, remaining important research aspects for future scientific efforts are formulated.

**Keywords** Extracorporeal life support (ECLS); Extracorporeal membrane oxygenation (ECMO); Cardiac and circulatory failure; Guideline; Recommendation

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\*Correspondence to: Prof. Dr. med. Alexander Assmann, Department of Cardiac Surgery, Heinrich Heine University, Medical Faculty, Moorenstr. 5, 40225 Düsseldorf, Germany. Tel: +49-(0)211-81-18331; Fax: +49-(0)211-81-18333. Email: alexander.assmann@med.uni-duesseldorf.de

<sup>†</sup>These authors contributed equally to the article.

## Introduction

Worldwide applications of extracorporeal circulation for mechanical support in cardiac and circulatory failure, which are referred to as extracorporeal life support (ECLS) or veno-arterial extracorporeal membrane oxygenation (va-ECMO), have dramatically increased over the past decade (in Germany from <300 cases in 2010 to 2852 in 2020).<sup>1,2</sup> In spite of the expanding use and the immense medical as well as socio-economic impact of this potentially life-saving, yet invasive and resource-demanding therapy, there has been a lack of interdisciplinary recommendations considering the best available evidence for ECLS treatment. In this context, a nationwide survey has previously underlined the heterogeneity in structural organization, conceptualization, technical application, and aftercare between the participating institutions.<sup>3</sup>

The success of ECLS therapy is based upon an effective teamwork involving experts of various medical professions and disciplines that are required to enable best possible decision-making concerning indication, therapy, and complication management, as well as weaning and aftercare. Therefore, the organization of structural and personnel resources is of great importance as well. Addressing all aforementioned aspects, the present clinical practice S3 guideline aims at the definition of recommendations based on the best available scientific evidence, thereby supporting clinicians when applying this complex therapy as well as elucidating important research questions to be answered.

## Methods

### Guideline development and design

The multiprofessional guideline group, led by the German Society for Thoracic and Cardiovascular Surgery (GSTCVS), comprised mandate holders of 16 scientific societies, a patients' representative (Supporting Information, *Table S1*), as well as an independent guideline methodologist. All recommenda-

tions were developed and passed in six well-structured consensus conferences applying the nominal group process under supervision of the AWMF (Association of the Scientific Medical Societies in Germany), explained in detail in the guideline report.<sup>4</sup>

### Aim and addressees of the guideline

The present S3 guideline aims at the implementation of evidence-based and consensus-based recommendations on the best available quality of care for patients requiring ECLS/ECMO support due to acute cardiac and circulatory failure. First-line addressees of the guideline are clinicians, nursing staff, and perfusionists who are involved in the treatment of patients with acute heart and circulatory failure, particularly in the areas of cardiac surgery, cardiology, intensive care medicine, emergency medicine, pneumology, trauma surgery, and paediatrics. Due to the special aspects of ECLS/ECMO in paediatrics, the recommendations for newborns, infants, and children are not described in this manuscript. Specific guideline content is relevant also for clinicians in rehabilitation institutions, physiotherapists, paramedics, as well as patients and their relatives.

### Evidence evaluation and grading of recommendations

The primary literature search (PubMed, Cochrane Library, CINAHL, EMBASE, G-I-N, AHRQ, ELSO website, and ClinicalTrials.gov) covered all related publications from 2010 to 2018 (9801 hits). Out of these, 68 articles (37 primary studies addressing efficacy, 27 registry studies including >1000 patients, and 4 secondary studies) fulfilled the obligate evidence criteria (*Figure S1*).<sup>4</sup> The levels of evidence (*Table 1*) for the different aspects of ECLS application were systematically assigned according to the GRADE (Grading of Recommendations Assessment, Development and Evaluation) criteria.<sup>5</sup> Based on the existing evidence, recommendations

Table 1 Levels of evidence

Level	Definition
++++	We are very confident that the true effect lies close to that of the estimate of the effect.
+++	We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.
++	Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect.
+	We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of the effect.
EC	Experts' consensus (evidence yet unclear).

were defined and graded (Table 2) in a well-structured consensus process.<sup>6</sup>

## Results

### General comments

In total, 71 recommendations on ECLS therapy in acute cardiac and circulatory failure were passed addressing the following categories: indications and contraindications, structural and personnel requirements, therapy management and monitoring, complication management, weaning, and after-care. The majority of recommendations (76%) relies on expert consensus, because only for the minority of ECLS therapy aspects, high-level evidence exists.

### Indications and contraindications

As cardiac and circulatory failure may occur in a heterogeneous group of patients with diverse and complex cardiovascular morbidity profiles, the decision on ECLS initiation should be made for each individual patient by the ECLS team, considering pro and contra criteria in the clinical context. However, based on the best available evidence, the following advice on indications is recommended.

Extracorporeal life support therapy is a last-line option that may be considered to improve the haemodynamics in shock scenarios particularly due to cardiac failure. For patients

requiring resuscitation due to in-hospital (IHCA) or out-of-hospital cardiac arrest (OHCA), a propensity-matched meta-analysis including nine studies has demonstrated a 30 day survival benefit for ECLS treatment versus conventional cardiopulmonary resuscitation [risk difference 14%; 95% confidence interval (CI) 2–25%;  $P = 0.02$ ] as well as improved 30 day survival with favourable neurological outcome, that is, Pittsburgh Cerebral Performance Category (CPC) 1 or 2 (risk difference 13%; 95% CI 7–20%;  $P = 0.0001$ ).<sup>7</sup> Heterogeneous patients' characteristics in the study populations with cardiac arrest result in a low grade of recommendation.

After resuscitation due to drug-induced toxic shock, the in-hospital mortality has been reported to be decreased under ECLS support as compared with conventional resuscitation [odds ratio (OR) 0.18; 95% CI 0.03–0.96;  $P = 0.04$ ].<sup>8</sup> Therefore, ECLS may be considered in these patients. For other shock scenarios, the currently available evidence does not suffice to allow for recommendations. In any case, if ECLS therapy is considered, it should be initiated early.

With regard to patients' age as a potential contraindication for ECLS therapy, registry studies from Taiwan as well as from the Extracorporeal Life Support Organization (ELSO) registry revealed a positive correlation between mortality and rising age, whereas cut-off values could not be determined. For this reason, patients' age currently cannot be defined as contraindication for ECLS therapy.<sup>9–12</sup> However, restrictions in ECLS initiation may be considered in patients at advanced age (octogenarians or nonagenarians) and/or after prolonged unsuccessful cardiopulmonary resuscitation.

All related recommendations of the guideline panel are presented in Table 3.

Table 2 Grades of recommendation

Recommendation	Symbol	Wording	Implication
Strong (negative) recommendation	↑↑/↓↓	'Shall'/'shall not'	>90% of patients would decide in favour of it/against it or benefit/not benefit from it or even be harmed by it.
(Negative) recommendation	↑/↓	'Should'/'should not'	Approximately 60% of patients would decide in favour of it/against it or benefit/not benefit from it or even be harmed by it.
Recommendation open	↔	'May' or 'unclear'	No conclusive study results are available to prove a beneficial or harmful effect.

Table 3 Indications and contraindications

Recommendation	Grade	Level
The decision on ECLS initiation 'should' be made individually by the ECLS team, considering pro and contra criteria in the clinical context. <sup>13</sup>	↑	EC
In cardiogenic shock, ECLS therapy 'may' be considered. <sup>7,14–17</sup>	↔	+ / + +
In in-hospital cardiac arrest, ECLS therapy 'may' be considered in individual cases. <sup>18–21</sup>	↔	+ + +
The decision pro ECLS 'should' be made early.	↑	+ + +
In out-of-hospital cardiac arrest, ECLS therapy 'may' be considered in individual cases. <sup>22–24</sup>	↔	+ + / + + +
The decision pro ECLS 'should' be made early.	↑	+ + / + + +
In order to avoid cardiocirculatory failure after cardiac surgery, the indication for ECLS initiation 'should' be evaluated intraoperatively.	↑	EC
In (drug-induced) toxic shock, ECLS therapy 'may' be considered. <sup>8</sup>	↔	+
Restrictions in ECLS initiation 'may' be considered in late elderly patients and after prolonged unsuccessful cardiopulmonary resuscitation. <sup>9–12</sup>	↔	+

### Structural and personnel requirements

Because the outcome of ECLS therapy in shock patients, representing the majority of indications, is strongly influenced by rapid ECLS installation without complications, the local expertise of the ECLS team is supposed to be crucial. ELSO registry data from 10 588 adult ECMO patients between 1989 and 2013 showed decreased mortality in high-volume centres, whereat more than 30 patients per year were beneficial concerning ECMO in general (OR 0.61; 95% CI 0.48–0.79;  $P < 0.001$ ), and in ECLS patients in particular (OR 0.39; 95% CI 0.29–0.53;  $P < 0.001$ ).<sup>25</sup> If ECLS therapy is applied with limited experience, the risk of significant patient damage is high. Therefore, the institution-related expertise, allowing for adequate identification of indications and management of the therapy including its complications, respectively, has to be ensured. However, the existing data do not support a minimum quantity of patients or procedures. Furthermore, the guideline group is aware of the issue that due to a definition of minimum quantity limits, unwarranted ECLS implantation may become attractive for low-volume centres. Nevertheless, the expert panel of this guideline considers a number of 20 ECLS patients per year as the minimum that should be aspired to.

Experience in ECLS initiation, continuation, weaning, and aftercare is more important than a physician's affiliation. Nevertheless, personnel exhibiting the standards of consultants in cardiac surgery, cardiology, anaesthesiology, and intensive care medicine as well as the qualification of a clinical perfusionist shall be involved in ECLS initiation and continuation. ECLS training for the multiprofessional team shall be conducted periodically according to an institutional curriculum.

Extracorporeal life support initiation shall be guided by locally adapted written standard operating procedures. Technically, all devices and material for ECLS implantation shall be available, including vascular sonography or angiography and

transoesophageal echocardiography, blood gas analysis, bronchoscopy, and the option to revise the femoral vessels surgically. A primed ECLS system and an additional backup system should be provided. All staff members involved in ECLS initiation shall be theoretically and practically trained in all aspects of ECLS therapy. If the structural, technical, and personnel requirement cannot be met, a collaboration with a 24/7 mobile ECLS team should be implemented. In an observational study on 210 patients with cardiogenic shock, mobile ECLS implantation yielded similar mortality at discharge when compared with ECLS initiation in an ECLS centre (OR 1.48; 95% CI 0.72–3.00;  $P = 0.29$ ).<sup>26</sup> Because complications during mobile ECLS transports occur frequently,<sup>27</sup> only experienced ECLS teams should transfer patients under mechanical circulatory support.

Extracorporeal life support continuation is strongly recommended to be performed only in ECLS centres with excellent interdisciplinary and multiprofessional expertise particularly in cardiac diseases and complex therapies in intensive care medicine, also ensuring 24/7/52 percutaneous coronary intervention and computed tomography.<sup>28,29</sup> During ongoing ECLS, timely consultation of each discipline required for the management of potential adverse events, such as vascular, neurological, or visceral complications, shall be available. Technical inspection of the ECLS system shall be conducted daily by a clinical perfusionist or another specially trained employee. Furthermore, the options of ventricular assist device implantation and heart transplantation listing should be available.

Non-physician staff, such as nurses with special expertise in intensive care and ECLS therapy,<sup>30</sup> clinical perfusionists, physiotherapists, palliative care specialists, institutional coordinators for ECLS/ECMO, or if required clerics, are integral part of the multiprofessional team enabling 'optimal' ECLS treatment.

All related recommendations of the guideline panel are presented in *Table 4*.

Table 4 Structural and personnel requirements

Recommendation	Grade	Level
<b>General structure</b>		
The exact minimum number of ECLS cases per year that allows for an adequate outcome is currently 'unclear'. <sup>25,31</sup>	↔	+
A minimum number of 20 ECLS cases per year 'should' be aspired to.	↑	EC
ECLS initiation, continuation, and training 'shall' be coordinated by the head physician of the ECLS programme according to institutional structures. <sup>13,28,29</sup>	↑↑	EC
ECLS training for the multiprofessional team 'shall' be conducted periodically according to an institutional curriculum. <sup>28</sup>	↑↑	EC
<b>ECLS initiation</b>		
ECLS initiation (indication + implantation) 'shall' be conducted by an experienced multiprofessional ECLS team, ideally in an ECLS expert centre. <sup>13,28</sup>	↑↑	EC
For ECLS initiation, specific equipment and structures 'shall' be provided. <sup>13,28</sup>	↑↑	EC
ECLS initiation 'shall' be guided by locally adapted written standard operating procedures. <sup>32</sup>	↑↑	EC
All staff members involved in ECLS initiation 'shall' be theoretically and practically trained in all aspects of ECLS therapy.	↑↑	EC
Hospitals without sufficient expertise 'should' implement a structured collaboration with an ECLS expert centre. <sup>13,28</sup>	↑	EC
The location of cardiac arrest (in-hospital or out-of-hospital) 'should not' significantly influence the decision on ECLS initiation.	↓	EC
Mobile ECLS teams 'should' be considered for ECLS initiation in individual cases in hospitals without ECLS expertise. <sup>26</sup>	↑	+
Out-of-hospital ECLS initiation 'may' be considered in individual cases.	↔	EC
Such cases 'should' be documented in a registry.	↑	EC
<b>ECLS continuation</b>		
ECLS continuation 'shall' be conducted on an ECLS-experienced intensive care unit, applying standardized, multiprofessional, multidisciplinary, and multimodal treatment concepts, headed by a consultant with additional qualification in intensive care medicine. <sup>28,29</sup>	↑↑	EC
During ECLS continuation, timely consultation of each discipline required for the management of potential complications 'shall' be available. <sup>28</sup>	↑↑	EC
The nurse-to-ECLS-patient ratio 'shall' be multidisciplinary defined per shift, considering the actual complexity. <sup>29</sup>	↑↑	EC
A nurse-to-ECLS-patient ratio of 1:1 'should' be possible if required.	↑	EC
Technical inspection of the ECLS system 'shall' be conducted daily by a perfusionist or another specially trained employee.	↑↑	EC

## Therapy management and monitoring

Although the evidence on effects by different types of ECLS pumps is quite low,<sup>33,34</sup> the successful clinical use over decades speaks in favour of centrifugal pumps, which shall be used for all ECLS applications, whereas the value of pulsatile flow cannot be judged on. For the choice of cannulation sites, the state of research does not allow for recommendations; however, it is addressed in the complication management section.

While there is no evidence on the ECLS anticoagulation strategies, the superior controllability and worldwide experience over decades lead unfractionated heparin as the anticoagulant of choice, frequently controlled by partial thromboplastin time or the activated clotting time measurements, thromboelastometry or factor Xa analysis.<sup>35–37</sup>

Furthermore, continuous or frequent monitoring of haemodynamics, organ perfusion, cardiac unloading, oxygenation,

neurological status, and functionality of the ECLS system shall be conducted. In case of femoral arterial cannulation, perfusion of the distal lower limb shall be monitored and oxygenation controlled by means of peripheral oxygen saturation measurement and arterial blood gas analyses both at the right upper extremity. Clinical neurological examination shall be conducted daily, and pupillometry several times a day.

All related recommendations of the guideline panel are presented in *Table 5*. In addition, parameters that shall be monitored during ECLS therapy are displayed in *Tables S2* and *S3*.

## Complication management

In order to detect complications early, continuous monitoring of haemodynamics, organ perfusion, cardiac unloading, oxy-

Table 5 Therapy management and monitoring

Recommendation	Grade	Level
<b>ECLS system and cannulation</b>		
Only centrifugal pumps 'shall' be used for ECLS. <sup>33,34</sup>	↑↑	+
The influence of pulsatile blood flow on the outcome is currently 'unclear'.	↔	EC
In case of inadequate decrease of elevated serum lactate levels or insufficient central venous oxygen saturation, a pump flow rate adaptation 'should' be considered.	↑	EC
The arterial cannulation site 'should' be chosen individually.	↑	EC
Peripheral ( <i>A. femoralis superficialis</i> ) or central cannulation ( <i>A. subclavia</i> , <i>Ao. ascendens</i> ) 'may' be conducted.	↔	EC
Coated ECLS components 'should' be preferred.	↑	EC
<b>ECLS anticoagulation and medication</b>		
For anticoagulation, unfractionated heparin 'should' be used.	↑	EC
After ECLS initiation, the catecholamine (particularly inotropes) dosage 'should' be reduced as much as possible.	↑	EC
<b>Concomitant therapy and sedation</b>		
Physiotherapy, respiratory training, and patient positioning 'should' be conducted.	↑	EC
Early patient mobilization 'should' be aspired to in experienced teams as long as the pump flow parameters remain stable.	↑	EC
Considering particularly safety, there 'should' be adequate analgesia, sedation as low as possible, and extubation if possible.	↑	EC
<b>Monitoring</b>		
Continuous or frequent monitoring of haemodynamics, organ perfusion, cardiac unloading, oxygenation, anticoagulation, neurological status, and functionality of the ECLS system 'shall' be conducted. <sup>38–40</sup>	↑↑	EC
In case of femoral arterial cannulation, oxygenation 'shall' be monitored by means of peripheral oxygen saturation measurement and arterial blood gas analyses both at the right upper extremity.	↑↑	EC
In case of femoral arterial cannulation, perfusion of the distal lower limb 'shall' be monitored.	↑↑	EC
Anticoagulation 'shall' be controlled frequently.	↑↑	EC
Clinical neurological examination 'shall' be conducted daily, and pupillometry several times a day.	↑↑	EC
The influence of additional automated neurological monitoring on the outcome is currently 'unclear'.	↔	EC

generation, anticoagulation, neurological status, and functionality of the ECLS system shall be conducted.

Infections frequently (10–30%) occur on ECLS, with increasing incidence in dependency on the duration of ECLS therapy, and negative impact on mortality.<sup>41,42</sup> In an ELSO registry study on 38 661 ECLS patients, it could be demonstrated that a pre-existing infection (diagnosed by positive blood cultures) was an independent predictor of infectious complications (OR 2.12; 95% CI 1.92–2.34;  $P < 0.001$ ).<sup>43</sup> Preventive strategies should aim at the avoidance of additional complications and consequent treatment of pre-existing infections. A verified infection shall be treated by antimicrobial medication prior to ECLS implantation, thereby not delaying urgent ECLS initiation.

The incidence of limb ischaemia on ECLS due to femoral or axillary cannulation has been reported up to 11–17%, and the probability of limb amputation up to 5%.<sup>42,44</sup> Pre-emptive implantation of an antegrade extremity perfusion cannula is an effective strategy to avoid limb ischaemia<sup>45</sup> and thus shall be performed. Furthermore, in case of femoral cannulation, the venous cannula should be implanted contralaterally to prevent venous backflow restrictions that may aggravate limb ischaemia.

Left ventricular distension, due to severely impaired myocardial contractility and ECLS-induced afterload, counteracts myocardial regeneration and supports complications such as intracavitary thrombus formation, pulmonary failure, and myocardial ischaemia.<sup>46</sup> Signs of left ventricular distension include pulmonary oedema (x-ray), left ventricular dilatation (echocardiography), and a diastolic pulmonary artery pressure  $> 25$  mmHg. If ventricular dilation cannot be resolved by conservative therapeutic measures, active mechanical unloading can and shall be achieved by a surgically or percutaneously introduced left ventricular or atrial vent catheter, a pulmonary arteria cannula, a transeptal atrioseptostomy, or implantation of an intra-aortic balloon pump or a left ventricular microaxial pump, respectively. An observational study in 48 cardiogenic shock patients showed an increased 30 day mortality if ECLS therapy was conducted without left ventricular unloading as compared with left ventricular vent insertion (OR 3.66; 95% CI 1.07–12.52;  $P = 0.038$ ).<sup>47</sup> The beneficial effect of a left ventricular microaxial pump has been demonstrated in two observational studies. One study on 63 ECLS patients showed decreased in-hospital mortality (OR 0.32; 95% CI 0.11–0.97;  $P = 0.04$ ),<sup>46</sup>

Table 6 Complication management

Recommendation	Grade	Level
In order to detect complications early, continuous monitoring of haemodynamics, organ perfusion, cardiac unloading, oxygenation, anticoagulation, neurological status, and functionality of the ECLS system 'shall' be conducted. <sup>11,41,43,49–54</sup>	↑↑	+
An existing infection 'shall' be treated by antimicrobial medication prior to ECLS implantation, thereby not delaying urgent ECLS initiation. <sup>43</sup>	↑↑	+
In case of femoral arterial cannulation, an antegrade perfusion cannula 'shall' be distally introduced to avoid lower limb ischaemia.	↑↑	EC
In case of femoral cannulation, the arterial and venous cannulas 'should' be introduced on different sides.	↑	EC
If left ventricular distension cannot be resolved by conservative measures, active mechanical unloading 'shall' be installed. <sup>46–48</sup>	↑↑	EC
Central hypoxia (watershed syndrome/harlequin syndrome) that occurs under ECLS therapy via femoral access and is refractory to conservative measures 'shall' be immediately treated by one of the following strategies: <ul style="list-style-type: none"> <li>• Change to a central arterial cannulation site (e.g. right axillary artery)</li> <li>• Insertion of an additional venous cannula (e.g. via the right internal jugular vein) and switchover to veno → arterio-venous ECMO</li> <li>• Insertion of an additional venous cannula (e.g. via the right internal jugular vein) and switchover to bi-veno → arterial ECMO</li> </ul>	↑↑	EC
If renal replacement therapy is required, a (semi-)continuous technique 'should' be applied to allow for optimized volume management.	↑	EC

while the other report on 66 ECLS patients demonstrated a decrease in 30 day (OR 0.40; 95% CI 0.19–0.84;  $P = 0.016$ ) and 1 year mortality (OR 0.39; 95% CI 0.19–0.81;  $P = 0.011$ ).<sup>48</sup>

Extracorporeal life support therapy in the presence of sustained left ventricular ejection results in a watershed-like phenomenon, which in case of femoral cannulation and insufficient pulmonary oxygenation can cause central hypoxia (harlequin syndrome). Thus, in order to early detect such a scenario, arterial blood gas analyses and continuous peripheral oxygenation measurement should be placed at the right upper extremity. Nevertheless, coronary ischaemia due to low left ventricular ejection may remain unidentified so that further impairment of the cardiac function and new onset of arrhythmias should be followed by respective examination. If central hypoxia under ECLS therapy via femoral access is refractory to conservative measures, it shall be immediately treated by one of the following strategies: change to a central arterial cannulation site (e.g. right axillary artery), insertion of an additional venous cannula (e.g. via the right internal jugular vein) and switchover to veno → arterio-venous ECLS, or insertion of an additional venous cannula (e.g. via the right internal jugular vein) and switchover to bi-veno → arterial ECLS.

All related recommendations of the guideline panel are presented in *Table 6*. The probability of typical ECLS complications is displayed in *Table S4*.

## Weaning

Attempts of weaning from ECLS succeed in only 30–70%,<sup>55–62</sup> so that the definition of criteria for successful weaning is

even more noteworthy. After general bridge-to-recovery candidacy is attributed, weaning may be considered at the earliest 48–72 h after implantation to allow for restoration of the myocardial function.<sup>63</sup> Strictly following a protocol, weaning should be started only if the following criteria are fulfilled: pulsatile arterial blood pressure and biventricular contractility, mean arterial blood pressure > 60 mmHg, venous (central venous) oxygen saturation  $\geq 65\%$  ( $\geq 60\%$ ), serum lactate normal ( $\leq 2$  mmol L<sup>-1</sup>) or decreasing, vasopressor and inotrope dosages low or decreasing, sufficient pulmonary oxygenation and CO<sub>2</sub> elimination under lung-protective ventilation, and compensated organ function (particularly liver function, while renal replacement therapy does not exclude successful weaning). Prior to ECLS explantation, the aforementioned criteria should be fulfilled under low ECLS blood flow (<2 L min<sup>-1</sup>) and low gas flow (<2 L min<sup>-1</sup>).

During weaning, the monitoring should especially comprise basic haemodynamic parameters (heart rate, arterial blood pressure, recapillarization time, and urine excretion), catecholamine dosage, lactate levels, echocardiography findings, pulmonary parameters [respiratory frequency, peripheral (right upper limb) oxygen saturation, and blood gas analyses], and chest x-ray. If required, more invasive haemodynamic monitoring (central venous pressure and oxygen saturation, pulmonary artery diastolic and occlusion pressure, and mixed venous oxygen saturation) should be applied. After every reduction of the ECLS blood flow (approximately 30 min later), arterial and venous blood gas analyses shall be evaluated to control the cardiocirculatory and pulmonary gas exchange function.

Inotrope administration may support the weaning process by improvement of the myocardial contractility. In a

Table 7 Weaning

Recommendation	Grade	Level
<b>ECLS weaning process</b>		
Prior to weaning from ECLS following a standardized protocol, the following criteria 'should' be fulfilled <sup>63,70</sup> :	↑	+
<ul style="list-style-type: none"> <li>• Pulsatile arterial blood pressure and echocardiographically biventricular contractility</li> <li>• Mean arterial blood pressure &gt; 60 mmHg</li> <li>• Venous (central venous) oxygen saturation ≥ 65% (≥60%)</li> <li>• Serum lactate normal (≤2 mmol L<sup>-1</sup>) or decreasing</li> <li>• Vasopressor and inotrope dosages low or decreasing</li> <li>• Sufficient pulmonary oxygenation and CO<sub>2</sub> elimination under lung-protective ventilation</li> <li>• Compensated organ function (particularly liver function, while renal replacement therapy does not exclude successful weaning)</li> </ul>		
Prior to ECLS explantation, the aforementioned criteria should be fulfilled under low ECLS blood flow (<2 L min <sup>-1</sup> ) and low gas flow (<2 L min <sup>-1</sup> ).	↑	+
After every reduction of the ECLS blood flow (approximately 30 min later), arterial and venous blood gas analyses 'shall' be evaluated to control the cardiocirculatory and pulmonary gas exchange function. <sup>38,39</sup>	↑↑	EC
In complex weaning scenarios, invasive monitoring by means of right heart catheterization 'may' be supportive.	↔	EC
Levosimendan 'may' beneficially influence the ECLS weaning. <sup>64</sup>	↔	++
Additional mechanical circulatory support systems 'shall not' be routinely used to support weaning from ECLS. <sup>46,65-69</sup>	↓↓	+
The influence of additional intra-aortic balloon pumps or microaxial pumps on the outcome during ECLS therapy is currently 'unclear'.	↔	EC
If an intra-aortic balloon pump or a microaxial pump has been implanted prior to ECLS initiation, the system 'may' be sustained during ECLS.	↔	EC
After unsuccessful weaning from ECLS, permanent ventricular assist device implantation 'should' be considered, consulting a ventricular assist device expert centre.	↑	EC
Optimal timing for the change from ECLS to a ventricular assist device is currently 'unclear'. <sup>71,72</sup>	↔	+
<b>ECLS explantation</b>		
After open surgical cannulation, cannula explantation 'should' be conducted also surgically, whereat the choice of surgical techniques (e.g. direct suture, patch, prosthesis ligation, and thrombectomy) is defined by the local findings.	↑	EC
After percutaneous cannulation, cannula explantation 'should' be conducted by manual compression, by means of percutaneous closure devices, or surgically, each in dependency on patient-specific and procedure-specific characteristics (e.g. cannula size, issues during cannulation, vessel size, peripheral arterial disease, and bleeding).	↑	EC
The decannulation technique 'should not' be chosen based on the length of the treatment period.	↓	EC
Therapy limitations and end-of-life decisions 'shall' be patient centred, adopted by the multiprofessional ECLS team, considering medical as well as ethical aspects, and adequately be communicated with the patients' relatives. <sup>73-75</sup> Such a scenario occurs, if the original therapeutic goal cannot be reached, is refused by the patient, or would be accompanied by stress that is not justified by the anticipated quality of life. <sup>76</sup>	↑↑	EC

single-centre study on 240 ECLS patients after cardiac surgery, levosimendan treatment decreased the risk of weaning failure (adjusted hazard ratio 0.41; 95% CI 0.22–0.8;  $P = 0.008$ ), the 30 day mortality (adjusted hazard ratio 0.52; 95% CI 0.30–0.89;  $P = 0.016$ ), and long-term mortality (adjusted hazard ratio 0.64; 95% CI 0.42–0.98;  $P = 0.04$ ).<sup>64</sup>

Additional mechanical circulatory support, particularly intra-aortic balloon pumps and left ventricular microaxial pumps, may be considered to support ECLS therapy and weaning. While routine implantation is not recommended, the following scenarios enable additional mechanical support: device implantation prior to ECLS escalation, additional device under ECLS to unload the left ventricle, or

additional device under ECLS to continue deescalated mechanical support after ECLS explantation. For an additional intra-aortic balloon pump support, literature reports are contradictory and thus do not lead to a recommendation aiming at outcome improvement,<sup>65-69</sup> whereas morbidity and mortality do not increase either, so a pre-implanted device may be sustained. While the routine use of additional microaxial pumps currently cannot be recommended, beneficial effects in case of left ventricular distension have been demonstrated.

After unsuccessful weaning from ECLS, permanent ventricular assist device implantation should be considered, consulting a ventricular assist device expert centre, whereas the



optimal timing for switching from ECLS to a permanent ventricular assist device is currently unclear.

Therapy limitations and end-of-life decisions shall be patient centred, adopted by the multiprofessional ECLS team, considering medical as well as ethical aspects, and adequately be communicated with the patients' relatives. Such a scenario occurs, if the initial therapeutic goal is unreachable, is refused by the patient, or would be accompanied by stress that is not justified by the anticipated quality of life.

All related recommendations of the guideline panel are presented in *Table 7*.

## Aftercare

Early after ECLS explantation, intensive care patients shall undergo continuous haemodynamic monitoring (invasive arterial blood pressure and oxygenation), as well as organ perfusion monitoring. Echocardiography shall be conducted directly after ECLS explantation, followed by daily examinations in the early phase, and in case of cardiopulmonary insufficiency. In addition, clinical examinations of the cannulation site shall be conducted at least once a day, and routine sonography of the cannulated vessels should be performed.

Standard care patients after ECLS explantation shall be daily evaluated particularly in terms of cardiac decompensation and cannulation-associated complications (e.g. infection, thrombosis, or ischaemia), naturally in addition to the general standard care supply. Besides inpatient rehabilitation programmes that all patients after ECLS should undergo, ambulatory aftercare is of outstanding importance. Frequent cardiological visits, preferably in a heart failure consultation, should be obligatory for patients with chronic cardiac insufficiency, especially for those after cardiogenic shock requiring ECLS therapy. Moreover, prolonged intensive care therapy can induce chronic disease (post-intensive care syndrome), such as psychiatric

syndromes, cognitive disorders, muscular dystrophy, hearing or sight disorders, or dysphagia, which severely impair patients' quality of life. Post-intensive care syndrome patients should be treated in the long term in ambulatory centres specialized on intensive care follow-up therapy.

All recommendations of the guideline panel are presented in *Table 8*.

## Discussion

In an interdisciplinary and multiprofessional approach, involving all scientific societies who take care of patients with acute cardiac and circulatory failure, the first evidence-based and expert consensus-based guideline on ECLS therapy has been created. This article presents all recommendations created by the expert panel, addressing multiple aspects of ECLS initiation, continuation, weaning, and aftercare as well as structural and personnel requirements, and thus should be used to apply the best standard of care nationwide.

In ECLS patients, the highest levels of evidence either cannot be generated or are not yet available. Nevertheless, the best available evidence has been systematically analysed, and consensus has been achieved in a multidisciplinary expert team following a well-structured process, so the final set of recommendations fulfils all criteria of a Level 3 guideline, which represents the highest guideline standard of the AWMF.

The limited availability of evidence clearly indicates the urgent need for further research for all aspects of ECLS. Because a low count of patients per institution and further study design issues, such as patient randomization in acute cardiac failure, impair the generation of high-quality evidence within reasonable time periods, particularly multi-centre efforts are encouraged. The present guideline aims to serve as reference supporting the definition of future research questions in such collaborative efforts.

**Table 8** Aftercare

Recommendation	Grade	Level
Intensive care patients early after ECLS explantation 'shall' undergo continuous monitoring of the haemodynamics (invasive arterial blood pressure measurement) and oxygenation, as well as organ perfusion monitoring.	↑↑	EC
Echocardiography 'shall' be conducted directly after ECLS explantation, daily in the early phase after explantation, and in case of cardiopulmonary insufficiency.	↑↑	EC
Early after decannulation of a peripherally cannulated ECLS system, clinical examination of the cannulation site 'shall' be conducted at least once a day, and routine sonography of the cannulated vessels should be performed.	↑↑	EC
Normal care patients after ECLS explantation 'shall' be daily evaluated particularly in terms of signs of cardiac decompensation and cannulation-associated complications (e.g. infection, thrombosis, or ischaemia), not disregarding the regular normal care examination.	↑↑	EC
Patients after ECLS therapy 'shall' undergo inpatient rehabilitation.	↑↑	EC
After discharge, ECLS patients 'shall' frequently visit a cardiological or specialized interdisciplinary outpatient unit, depending on the complexity of the disease.	↑↑	EC

While there exists some evidence on the indications for ECLS therapy, the data on contraindications are modest. This is all the more noteworthy, because in emergency situations, the decision against ECLS rescue therapy is frequently more difficult than just the technical device implantation. Thus, in spite of complexity and potential ethical issues regarding the study design, it is of great interest—from a patient-centred as well as from a health economics point of view—to generate high-quality evidence particularly on ECLS contraindications.

The aspect of minimum quantities in this context is a matter of controversial debate, especially as the actual patient numbers are quite low in the majority of applying institutions compared with other invasive therapies. Future research may focus on personnel, process, and structural requirements that allow for safe ECLS therapy with adequate outcome.

Left ventricular distension and central hypoxia due to the watershed phenomenon are common ECLS complications that can suddenly occur and have to be counteracted urgently. Because effective treatment is crucial with regard to the potential for myocardial vitality and regeneration as well as the avoidance of cerebral damage, more evidence on the impact of different treatment strategies is desirable.

There is also need for research on weaning approaches including predictors in this context. Especially the effect of pharmacological weaning support by levosimendan or additional mechanical circulatory support by microaxial pumps may be evaluated, because clinical observations speak in favour of these strategies; however, the evidence is yet unclear. Furthermore, the usefulness of vascular closure devices to support cannula explantation should be addressed.

Neither clinical nor ambulatory aftercare nor rehabilitation programmes are currently based on evidence. Because patients after ECLS therapy regularly suffer from chronic cardiac sufficiency, research on the optimization of aftercare and rehabilitation is all the more warranted.

## Limitations

The guideline panel consisted of experts from Germany, Austria, and Switzerland. Generally, structural and personnel requirements for ECLS therapy may be defined differently in other health care systems. However, the panel aspired to define universal requirements, which may be transferred to health care systems with different resources and specializations. All other aspects of ECLS therapy were addressed by medical recommendations that represent the best available standard of care independently of the health care system in which they should be applied.

## Validity and update

These guideline recommendations are based on the best scientific advice that is currently available for each of the aspects of ECLS therapy. The guidelines were approved by the mandate holders of all participating scientific societies. They are valid up to August 2025.

The full version of the guideline in German language including all background information as well as recommendations on ECLS therapy in paediatric patients is available from <https://www.awmf.org/leitlinien/detail/II/011-021.html>.

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## Conflict of interest

None declared.

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## Supporting information

Additional supporting information may be found online in the Supporting Information section at the end of the article.

**Figure S1.** PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) flow chart displaying the literature selection process.<sup>1</sup> \*guideline databases (G-I-N, AHRQ), ELSO (extracorporeal life support organization) website and ClinicalTrials.gov. \*\*considered for consensus questions and background information.

**Table S1.** Composition of the guideline group.

**Table S2.** Patient monitoring parameters.

**Table S3.** ECLS monitoring parameters.

**Table S4.** Incidence of ECLS complications.

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