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REVIEW

# Recommendations for extracorporeal cardiopulmonary resuscitation (eCPR): consensus statement of DGIIN, DGK, DGTHG, DGfK, DGNI, DGAI, DIVI and GRC

**Guido Michels[1,23] · Tobias Wengenmayer[2,23] · Christian Hagl[3,24] · Christian Dohmen[4,25,26] · Bernd W. Böttiger[5,26,27,28] · Johann Bauersachs[6,29] · Andreas Markewitz[7,24,26] · Adrian Bauer[8,30] · Jan-Thorsten Gräsner[9,27,28] · Roman Pfister[1] · Alexander Ghanem[10] · Hans-Jörg Busch[11,23,26,28] · Uwe Kreimeier[12,26,28] · Andreas Beckmann[13,24] · Matthias Fischer[14,27] · Clemens Kill[15,27] · Uwe Janssens[16,23,26] · Stefan Kluge[17,23,26] · Frank Born[3,30] · Hans Martin Hoffmeister[18,29] · Michael Preusch[19] · Udo Boeken[20] · Reimer Riessen[21,23] · Holger Thiele[22,29]**

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**Abstract**
Extracorporeal cardiopulmonary resuscitation (eCPR) may be considered as a rescue attempt for highly selected patients with refractory cardiac arrest and potentially reversible aetiology. Currently, there are no randomised, controlled studies on eCPR. Thus, prospective validated predictors of benefit and outcome are lacking. Currently, selection criteria and procedure techniques differ across hospitals and standardised algorithms are lacking. Based on expert opinion, the present consensus statement provides a first standardised treatment algorithm for eCPR.

**Keywords** Cardiac arrest · Extracorporeal cardiopulmonary resuscitation · Extracorporeal membrane oxygenation · Cardiogenic shock · Resuscitation

## Introduction

At least 275,000 patients in Europe suffer an out-of-hospital cardiac arrest (OHCA) every year [1]. In the US, approximately 568,500 cardiac arrests occur annually. Of these, 359,400 (63%) occur outside hospital (OHCA) and 209,000 (37%) inside hospital (in-hospital cardiac arrest, IHCA) [2]. With 60%, cardiac aetiology is presumed to be the most common reason [3, 4]. In approximately 20–30% of cases, the origin is not cardiac [5, 6]. Even with immediate initiation of conventional cardiopulmonary resuscitation (CPR), survival rate with a favourable neurological outcome (mild to moderate neurological impairment, equivalent to a cerebral performance category (CPC) of 1–2) is low, both for IHCA and for OHCA [5–10% (OHCA) versus 15% (IHCA)] [7–9]. Extracorporeal cardiopulmonary resuscitation (eCPR) can be considered a rescue attempt for selected patients with refractory cardiac arrest of potentially reversible cause (e.g. myocardial infarction or pulmonary embolism) [10–12]. Observational studies suggest that eCPR can increase survival rate up to 30% in these patients [4, 13–22]. A meta-analysis showed an absolute increase of 30 day survival of 13% compared with conventional CPR (95% CI 6–20%; $p < 0.001$; number needed to treat 7.7) [23].

Currently, highly selected patients (see Table 1) receive venoarterial extracorporeal cardiovascular life support (VA-ECLS) under conventional or mechanical CPR [mCPR with, for instance, the LUCAS® (Physio-Control, Inc., Redmond, WA, USA) or AutoPulse® (ZOLL (Resuscitation Products), Chelmsford, MA, USA) system]. Selection criteria and procedures vary across institutions. Venoarterial extracorporeal membrane oxygenation (VA-ECMO) is commonly defined in the literature and in this consensus paper as being synonymous with extracorporeal life support system (ECLS) [24]. The present consensus paper offers a proposal for a standardised algorithm for eCPR with the use of an ECLS. The consensus paper has been written with representatives of the German Society

This consensus statement was also published in Medizinische Klinik—Intensivmedizin und Notfallmedizin, Der Kardiologe, Der Anaesthesist, Zeitschrift für Herz-, Thorax- und Gefäßchirurgie und Anästhesiologie and Intensivmedizin. The consensus paper is currently available in German only. This paper is the first English version of the eCPR German consensus statement.

✉ Guido Michels
guido.michels@uk-koeln.de

Extended author information available on the last page of the article

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of Medical Intensive Care and Emergency Medicine (DGIIN), the German Cardiac Society (DGK), the German Society of Thoracic, Cardiac and Vascular Surgery (DGTHG), the German Society of Cardiotechnics (DGfK), the German Society of Neuro-Intensive Care and Emergency Medicine (DGNI), the German Society of Anaesthesiology and Intensive Care Medicine (DGAI), the German Interdisciplinary Association for Intensive Care and Emergency Medicine [DIVI, section group Neurological Medicine (Studies and Standards in Neurological Medicine), the section group Emergency Medicine (Resuscitation and Post-Resuscitation Therapy), section group Ethics], and the German Resuscitation Council (GRC).

## Previous guidelines and recommendations

Neither the guidelines of the European Resuscitation Council [10] nor the guidelines of the American Heart Association [8] on CPR recommend the routine use of eCPR for patients with cardiac arrest [Class IIb (benefit ≥ risk), evidence level C-LD (limited data)]. A separate guideline on eCPR from the 'Extracorporeal Life Support Organisation (ELSO)' [26] is limited to general aspects of eCPR only.

## Current studies

Randomised controlled trials (RCT) on eCPR are lacking so far, and there are no prospectively validated criteria for selecting patients and determining indications for eCPR [27]. Defining predictors of risk and benefit, which could help to determine indications for eCPR, remain to be a major clinical challenge. A meta-analysis by Debaty et al. [19] investigated the prognostic value of various risk factors which might help guiding the specialist in acute settings when the question to initiate eCPR or not raises. Primary outcome was significantly better in the presence of an initially defibrillatable heart rhythm (OR 2.2, 95% CI 1.30–3.72, $p = 0.003$), a shorter low-flow time (time from CPR initiation to eCPR, geometric mean ratio 0.90, 95% CI 0.81–0.99, $p = 0.04$), a higher pH (Δ pH (arterial) 0.12, 95% CI 0.03–0.22, $p = 0.01$) and a low serum lactate concentration (Δ −3.52 mmol/L, 95% CI −5.05 to −1.99, $p < 0.001$).

Together with data from other major observational studies, a defibrillatable heart rhythm appears to be an important prognostic factor for patients with OHCA [19]. At present, however, it does not seem justified to deny eCPR categorically for patients without defibrillatable heart rhythms. The prognostic value of the low-flow time has already been documented, both for in-hospital and out-of-hospital cardiac arrest [19, 28]. The time factor seems to play a particularly important part. A Japanese registry study showed that strict adherence to the 'collapse-to-start eCPR' of < 40 min and the 'collapse-to-coronary reperfusion' of < 60 min was accompanied by the best prognostic outcome [29]. However, even in cities with established eCPR programmes, low-flow time to ECLS support exceeded 70 min. Analogous to the treatment of ST-segment elevation myocardial infarction it will be very important to reduce low-flow time in future [17, 28]. Current and future studies [e.g. the CAREECMO study (NCT0335299)] are investigating whether a considerably accelerated CPR algorithm for selected patients, with the focus on rapid transportation following the 'load-and-go' principle or preclinical ECLS initiation [30] have more impact on mortality. Moreover, early arrival of the first-aider, a low serum lactate, a higher $etCO_2$ before arrival at the cardiac catheterisation laboratory and the presence of coronary heart disease as a reversible cause for collapse are associated with a significantly higher probability of survival [31].

As biochemical markers, pH and serum lactate have emerged as 'the' prognostic factors at many sites [19]. However, any prolonged CPR causes deviations of pH and serum lactate levels, owing to a metabolic imbalance at cellular level. One-off elevations should therefore be interpreted with caution, whereas clearance might be more important over time [32, 33]. Comparing both markers, pH seems to predict neurological outcome better than lactate levels [34]. By the way, venous pH shows a good correlation with the arterial pH [35]. There are no well-validated cut-off values, neither for pH nor for serum lactate. These values of these parameters must be interpreted in clinical context only. In the past pH values below 6.8 were supposed to be incompatible with life, according to textbook opinion [36]. However, some current case reports show a good neurological outcome with even lower pH values (CPC 1–2) [37, 38]. Nevertheless, a retrospective analysis of prospective registry data of OHCA patients showed that a pH < 6.8 was not associated with a good neurological outcome [39].

Therefore, decision to initiate eCPR should always be made by a multi-professional 'eCPR team' (see Recommendation 2, below), taking into account all available indicators individually (Table 1). Besides these event-related variables, general patient-related, variables are also of prognostic significance. Obesity is often discussed in this context, as it might hinder the placement of ECLS cannula. However, a retrospective observational study showed that the body mass index (BMI < 18.5 to ≥ 30 kg/m$^2$) was not associated with either an increased mortality or a poorer neurological outcome in eCPR patients [40]. A retrospective study showed that the 1-year survival rate was significantly lower for patients with malignant disease than for those with non-malignant disease (1.7% versus 11.4%) [41]. Moreover, elderly and frail patients with OHCA show a low probability of survival [42]. Age itself does not seem to have a negative effect on the survival rate and therefore should not be

**Table 1** Possible decision criteria with regard to eCPR (adapted from Michels et al. [25])

| Pro criteria | Contra criteria |
|---|---|
| ■ Observed cardiac arrest | ■ Age > 75 years and frailty |
| ■ Presumed cardiac aetiology, especially defibrillatable initial heart rhythm | ■ Non-observed cardiac arrest<br>■ No-flow time ≥ 10 min |
| ■ No-flow time ≤ 5 min | ■ Clinical signs of severe irreversible brain damage or expected poor neurological prognosis |
| ■ Short low-flow time ≤ 60 min | ■ Inadequate resuscitation measures (e.g. absent, doubtful or intermittent resuscitation by lay responder/s) |
| ■ Consistently high-quality resuscitation measures (effective resuscitation by lay responder/s) | |
| ■ Presence of a reversible cause of the cardiac arrest (4 H's and HITS). This includes hypoxia, hypovolaemia, hypo- and hyperkalaemia (metabolic dysfunctions), accidental hypothermia, pericardial tamponade, intoxication, thromboembolism (myocardial infarction, pulmonary embolism) and tension pneumothorax | ■ Comorbidities with reduced life expectancy (e.g. underlying oncological condition under palliative care, terminal heart failure or COPD, advanced dementia)<br>■ Prolonged CPR of > 20 min in the case of asystole (exception: accidental hypothermia, intoxication, near-drowning and suspected pulmonary embolism) or of > 120 min in the case of persistent ventricular fibrillation/ventricular tachycardia<br>■ Low pH (< 6.8) and high lactate (> 20 mmol/L)<br>■ Patient's refusal (advance directive, the presence of emergency sheet regarding advance-care planning)<br>■ Contraindications to full anticoagulation (e.g. active bleeding, severe trauma or haemothorax after CPR) |

As the decision for or against eCPR should not depend solely on 'one' indication or 'one' contraindication, terms such as absolute or relative indication or contraindication have been deliberately avoided. No-flow time is defined as the time from the collapse event to the initiation of CPR; conversely, the low-flow time is defined as the interval from the start of CPR to the return of spontaneous circulation or onset of eCPR

*COPD* chronic obstructive pulmonary disease, *CPR* cardiopulmonary resuscitation

listed as an absolute contraindication [22, 43, 44]. In summary, observational studies have yielded a series of variables of prognostic significance—none of these markers can be regarded as a 'no-go' decision aid.

Although observational studies showed a survival advantage for eCPR over conventional CPR after IHCA and OHCA, RCT data are still missing. Some RCTs on this topic have recently been initiated [e.g. the INCEPTION study (NCT03101787, scheduled completion 2019), the EROCA study (NCT03065647, scheduled completion 2019), the Prague OHCA study (NCT01511666, scheduled completion 2018), and the ACPAR2 study (NCT02527031, scheduled completion 2018)], and until these studies are completed it will not be possible to make any statement about clinical endpoints.

Besides the medical aspects of eCPR, it is also necessary to consider the ethical aspects (such as diagnosis of brain death under ECLS) and the potential psychological burdens on the treatment team and the family [45–49].

## Treatment pathways—current evidence

### Out-of-hospital cardiac arrest (OHCA)

No standardised treatment pathway for patients under CPR has been clarified yet. Even in the case of a favourable ventricular rhythm event over 60% of the patients display refractory ventricular fibrillation and rarely achieve a return of spontaneous circulation (ROSC), or die before hospital admission [50]. In a prospective study by Yannopoulos et al. [31], an algorithm was established for selected patients with refractory ventricular fibrillation (age 18–75 years, transfer time < 30 min to the cardiac catheterisation lab, patients received at least three defibrillations and 300 mg of amiodarone without achieving ROSC). Patients in this specific group were transported rapidly to a 24-h/7-day/365-day hospital with readiness for cardiac catheterisation under mCPR (LUCAS® chest compression system). Placement of an ECLS was done immediately on arrival in the cardiac catheterisation laboratory if there were no specific exclusion criteria ($etCO_2$ < 10 mmHg, $p_aO_2$ < 50 mmHg or $SO_2$ < 85%, serum lactate > 18 mmol/L). Left-heart catheterisation, if necessary with coronary intervention was performed in the same setting. Certain patients were excluded from this rapid emergency transport: the presence of a cardiac arrest of non-cardiac aetiology (e.g. trauma, haemorrhage), contraindications to the placement of a LUCAS® device, known pregnancy, nursing home patients, the existence of a 'Do-Not Resuscitate/Do-Not Intubate' situation (e.g. an advance directive), and the presence of a terminal disease (e.g. cancer or terminal heart or kidney failure). 9% of the patients experienced ROSC on the way to the cardiac catheterisation laboratory, 91% of the patients (50/55) were cannulated for eCPR and 84% received a successful coronary intervention. Complications associated with ECLS placement were retroperitoneal bleeding (8%) and other vascular complications (6%). 42.0% of the patients survived with a

good neurological status (CPC 1–2) versus 15.3% in a historical comparison group. Fluoroscopy-guided cannulation of the femoral vessels under CPR conditions is safe [51] and leads to a reduction of complication rates without loss of time [52]. Up-to-date, there is no randomised controlled or prospective study comparing fluoroscopically guided with ultrasonically guided ECLS placement. A small retrospective single-centre observational study compared the cannulation time for anatomical 'landmark' based vessel puncture plus the use of conventional wires with that of ultrasound guided vessel puncture using stiff wires [53]. The median cannulation time was 17 (12–26) min (landmark technique) versus 8 (6–12) min (ultrasonic technique, $p < 0.001$), which favours the use of ultrasound and stiff wires. From an interventional point of view, the 'stiff-wire' method generally is the preferred procedure—irrespective of whether the landmark or the ultrasonic technique is used. In this study, cannulation was performed by interventional cardiologists only. Some answers to the question of the optimum cannulation method are still missing [53]. Given that early coronary angiography in resuscitated patients is accompanied by lower mortality [54, 55]—and as no other algorithm has yet been studied—the 'CPR-cardiac catheterisation pathway' should be preferred [31]. Direct transportation of selected patients with OHCA to a cardiac arrest centre with cardiac catheterisation readiness should be the aim [56, 57]. Hospitals with an ECMO/ECLS programme should be able to implant an ECLS at various sites in the hospital (e.g. the trauma room or cardiac catheterisation laboratory) [57]. This will ensure that an eCPR can be done even with non-cardiac aetiology (e.g. accidental hypothermia) [58].

### In-hospital cardiac arrest (IHCA)

The treatment pathways within hospital departments depend on the prevailing conditions and resources and therefore vary widely. In the case of IHCA, it might be appropriate to cannulate the patient an ECLS on the spot (e.g. in the intensive-care ward), to save transport time.

For hospitals without the structural and staffing requirements for ECLS placement, it is recommended to have predefined contact persons at the nearest hospital with an ECMO–ECLS programme. A brief discussion will reveal wether it is more advisable to rapidly transport the patient under CPR to ECLS centre or to send an ECLS team to the patient.

## Organisational requirements and recommendations for eCPR

1. Seamless eCPR readiness requires a 24-h/7-day/365-day availability of the eCPR team with correspondingly short assembly time.
2. The multi-professional eCPR team ideally consists of a doctor who is additionally qualified in emergency medicine or a medical specialist who is additionally qualified in intensive care medicine and the ECLS implantation team. The ECLS implantation team should meet medical specialist standards from at least two of the three specialities of cardiology, cardiac surgery and anaesthesiology and should also include a cardiovascular perfusionist, or—especially in institutions without a cardiovascular perfusion unit—a professional care staff specifically trained in ECLS with the qualifications listed in the following sentence. The assistants and/or nurses who are involved with implanting and operating the ECLS are trained nursing professionals—ideally with further specialist training in intensive or emergency nursing—and are experienced in the therapy of patients with ECLS. For further information, please consult the appropriate European recommendations [30].
3. The eCPR programme should ideally be attached to a hospital with an intensive-care unit and many years of experience in the care of ECLS patients and also the option of further treatments (for instance, the implantation of ventricular support systems or heart transplants) [30, 59].
4. Availability of portable ECLS/ECMO systems is not given all over Germany. For that, the patient should be admitted to a collaborating hospital with 24-h/7-day/365-day cardiac catheterisation and ECLS readiness. If mobile extracorporeal support systems are used, e.g. in patients with massive pulmonary embolism under CPR, please consult the recommendations for inter-hospital transfer under ECLS [60–62].
5. A telephone notification call and a shared checklist-based indication review should be made with the doctor responsible in the ECLS team. Ideally, the review should be done within the first 15 min of low-flow time (refractory CPR [20, 30]) und includes age, possible comorbidities, initial rhythm, no-flow time and ROSC status.
6. Valid procedural instructions must be implemented which reliably define the structured handover and the sites of intervention to improve and maintain communication between the parties [57].
7. After the structured handover (including team time-out), a general clinical examination and immediate focused ultrasound/echocardiography under mCPR should be done to rule out or detect any reversible causes (pneumothorax, signs of right ventricular strain indicating pulmonary embolism, pericardial tamponade, left ventricular dysfunction and hypovolaemia) [63–65].

8. The final decision about performing an ECLS placement should be made by the ECLS implantation team after weighing up the pro and contra criteria. Until then the CPR should be continued uninterruptedly and in accordance with the guidelines [66–68].
9. An arterial access should be installed for haemodynamic monitoring under CPR and to determine the chemical laboratory prognostic factors (serum lactate, pH). Ideally, an arterial catheter should be placed in the common femoral artery for this purpose immediately on arrival of the patient. Besides the arterial blood gas analysis and the invasive monitoring of blood pressure arterial cannulation for the ECLS can be performed at this site.
10. A separate intensive care or trauma team, consisting of a doctor with experience in the critical care of resuscitated patients (if possible > 1 year) and nursing staff should be present continuously during ECLS placement and take care of the hemodynamic and respiratory support as well monitoring.
11. A 'collapse-to-start eCPR interval' of 60 min [69] and a 'door-to-ECLS implantation time' of less than 30 min should be adhered to depending on local conditions [70].
12. The ECLS placement via the femoral artery (15–19 Fr) and femoral vein (19–23 Fr) should ideally be done either in the cardiac catheterisation laboratory under fluoroscopic guidance (if necessary by vascular ultrasound) or in the emergency department/trauma room under ultrasonic guidance [71, 72].
13. After ECLS placement a distally oriented catheter should be inserted for anterograde leg perfusion under ultrasonic guidance. If placement is unsuccessful and there are clinical or technical signs of critically low perfusion (e.g. via near-infrared spectroscopy on the lower leg) open surgical implantation should be persued. The correct site and functioning of the distally oriented catheter must be evaluated early by appropriate diagnostic methods (e.g. vascular ultrasound or (CT) angiography).
14. There should be a low threshold for considering a whole-body CT scan, depending on the clinical situation after ECLS placement, to identify undetected causes of cardiac arrest (especially central processes), secondary injuries after CPR and complications due to the ECLS placement [73].
15. Guideline-compliant temperature management (32–36 °C constantly for 24 h) should be carried out, taking into account the current blood coagulation status and bleeding complications [66, 74].
16. The additional implantation of a left ventricular microaxial pump [Impella® (Abiomed U.S., Danvers, MA, USA)] can be considered over time if there is no pulsatility or only minimal left ventricular contractility consistent with left ventricular unloading in the form of 'venting' [75, 76].
17. Prognostication in eCPR patients remains difficult. In particular, the question if and when an eCPR should be terminated should be decided—given the lack of scientific evidence to date—within the interdisciplinary intensive care and ECLS team, taking account of the medical and ethical aspects, as a decision specific to the patient as an individual. The current guidelines on resuscitation generally recommend a neurological prognosis assessment and treatment decision not earlier than 72 h after ROSC [10].
18. An eCPR process flowchart in the form of a standardised operating procedure (SOP) should be established in the eCPR team and evaluated at regular intervals (Fig. 1).

## Quality criteria

Besides technical skills, implementing eCPR requires social, economic and medical–ethical skills [69].

1. For the care of patients with pre-hospital cardiac arrest, please consult the quality indicators and structural requirements for 'cardiac arrest centres' [57].
2. Implementing eCPR demands considerable resources and requires very good communication and co-operation between all members and associates of the eCPR team—similar to regional infarct networks [77]. Especially, because of the great importance of early notification and shared eCPR assessment in the form of a 'rapid decision-making' process management and the focus on rapid transportation a close dialogue and binding structural collaboration with the local emergency medical services is essential.
3. Under the direction of a qualified mentor, a multi-professional training for team-focused eCPR contributes to quality assurance [78].
4. At regular meetings, quality criteria/features (e.g. optimising the eCPR-SOP), the current study results and case reports should be reported and discussed. Participation in national and international multicentre studies is desirable.
5. Since many undesirable events and complications arise from the complexity of treatment, uncertainty, lack of team management or misunderstandings between members of the eCPR team in the ad hoc emergency situation, all participants in the eCPR team should receive the appropriate quality of training and instruction. For that reason, there should be clearcut rules governing the

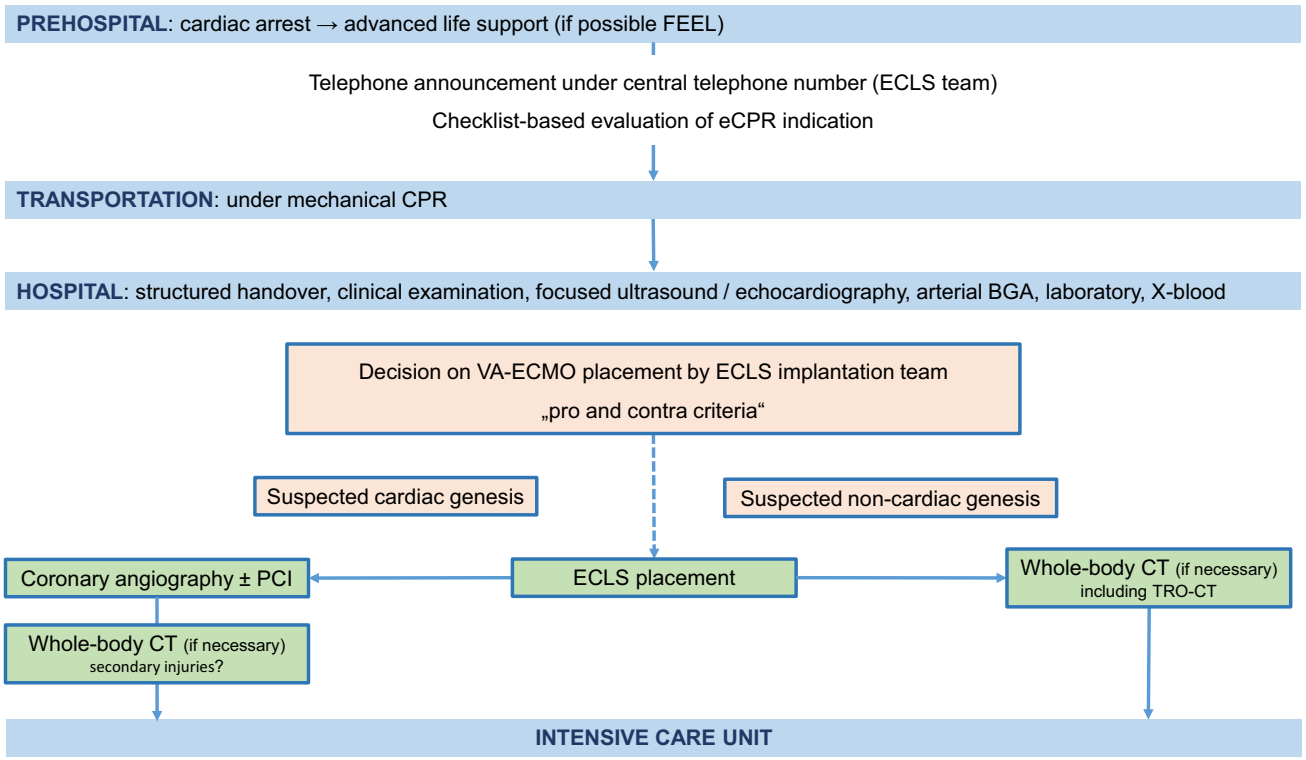


**Fig. 1** eCPR algorithm. *BGA* blood gas analysis, *CPR* cardiopulmonary resuscitation, *CT* computed tomography, *ECMO* extracorporeal membrane oxygenation, *ECLS* extracorporeal life support system, *eCPR* extracorporeal cardiopulmonary resuscitation, *FEEL* focused echocardiographic evaluation in life support, *PCI* percutaneous coronary intervention, *TRO-CT* triple-rule-out CT angiography, to rule out or detect simultaneously coronary heart disease, an acute pulmonary embolism and acute aortic disease, *VA* venoarterial, *X-blood* blood for cross-match

allocation of responsibilities with regard to both medicine and logistics, and training sessions should be held regularly.

6. To achieve the appropriate quality, the requirement is a caseload of at least 30 ECLS/ECMO placements (elective plus under CPR) per year and per hospital with an ECMO/ECLS programme [30, 79].
7. To maintain quality in line with current recommendations and study data, the aim is to update this present consensus paper every 5 years.

## Compliance with ethical standards

**Conflict of interest** Michels G is a member of the scientific advisory board of the German Society of Medical Intensive Care and Emergency Medicine (Deutsche Gesellschaft für Internistische Intensivmedizin und Notfallmedizin, DGIIN), commissionery leader of the working group of "Cardiopulmonary Resuscitation" of the German Society for Cardiology (Deutsche Gesellschaft für Kardiologie, DGK) and member of the working group "ECMO / eCPR" of the German Resuscitation Council (GRC) and received lecture fees from Pfizer, Novartis, Servier, ZOLL and Orion Pharma. Bauersachs J is the leader of the DFG-funded Clinical Research Group (KFO) 311 "(Pre) terminal heart and lung failure: Relief and Repair" and received lecture fees and research support from Abiomed and ZOLL. Böttiger BW is European Resuscitation Council (ERC) Board Director Science and Research, chairman of the German Resuscitation Council (GRC), member of the "Advanced Cardiac Life Support" (ALS) Task Force of the International Liaison Committee on Resuscitation (ILCOR), member of the presidium of the German Interdisciplinary Association for Intensive Care and Emergency Medicine (Deutsche Interdisziplinäre Vereinigung für Intensiv- und Notfallmedizin, DIVI), associated editor of the European Journal of Anaesthesiology (EJA), co-editor of the journal Resuscitation, editor of the journal Notfall + Rettungsmedizin. For lectures he has received fees from the following companies: Medupdate, Forum for Medical Education (FoMF), Baxalta, Bayer Vita, ZOLL, BARD. Ghanem A has received lecture fees from Getinge. Markewitz A received a lecture fee from TÜV Süd, München. Gräsner JT is the leader of the scientific working group "emergency medicine" of the German Society of Anaesthesiology and Intensive Care Medicine (Deutsche Gesellschaft für Anästhesiologie und Intensivmedizin, DGAI), speaker of the organizing committee of the "German Reanimation Registry", Chair of the European Registry of Cardiac Arrest, member of the executive committee of the German Council for Resuscitation (GRC), member of the presidium of the professional association of german anaesthesiologists. Kreimeier U is leader of the working group "Advanced Life Support" at the German Resuscitation Council (GRC). Wengenmayer T, Hagl C, Dohmen C, Bauer A, Pfister R, Busch HJ, Beckmann A, Fischer M, Kill C, Janssens U, Kluge S, Born F, Hoffmeister HM, Preusch M, Boeken U, Riessen R and Thiele

H declare, that there is no conflict of interest with respect to the subject publication.

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## Affiliations

**Guido Michels[1,23] · Tobias Wengenmayer[2,23] · Christian Hagl[3,24] · Christian Dohmen[4,25,26] · Bernd W. Böttiger[5,26,27,28] · Johann Bauersachs[6,29] · Andreas Markewitz[7,24,26] · Adrian Bauer[8,30] · Jan-Thorsten Gräsner[9,27,28] · Roman Pfister[1] · Alexander Ghanem[10] · Hans-Jörg Busch[11,23,26,28] · Uwe Kreimeier[12,26,28] · Andreas Beckmann[13,24] · Matthias Fischer[14,27] · Clemens Kill[15,27] · Uwe Janssens[16,23,26] · Stefan Kluge[17,23,26] · Frank Born[3,30] · Hans Martin Hoffmeister[18,29] · Michael Preusch[19] · Udo Boeken[20] · Reimer Riessen[21,23] · Holger Thiele[22,29]**

1 Department III of Internal Medicine, Heart Centre of the University of Cologne, Kerpener Str. 62, 50937 Cologne, Germany

2 Department of Cardiology and Angiology I, Heart Center Freiburg University, Faculty of Medicine, University of Freiburg, Freiburg, Germany

3 Department of Cardiac Surgery, Ludwig-Maximilians-University Munich, Munich, Germany

4 LVR-Hospital Bonn, Bonn, Germany

5 Department of Anaesthesiology and Intensive Care Medicine, University Hospital of Cologne, Cologne, Germany

6 Department of Cardiology and Angiology, Hannover Medical School, Hannover, Germany

7 Bendorf, Germany

8 Department of Cardiovascular Perfusion, MediClin Heart Center Coswig, Coswig, Saxony-Anhalt, Germany

9 Institute for Emergency Medicine, University Hospital Schleswig-Holstein, Kiel, Germany

10 Department of Cardiology, Asklepios Klinik St Georg, Hamburg, Germany

11 Department of Emergency Medicine, University Hospital of Freiburg, Faculty of Medicine, University of Freiburg, Freiburg, Germany

12 Department of Anaesthesiology, Ludwig-Maximilians-University Munich, Munich, Germany

13 Department of Cardiac Surgery, Heart Centre Duisburg, Evangelisches Krankenhaus Niederrhein, Duisburg, Germany

14 Department of Anaesthesiology, Intensive Care Medicine, Emergency Medicine and Pain Service, Hospital Am Eichert, Alb Fils Kliniken GmbH, Goeppingen, Germany

15 Centre of Emergency Medicine, University Hospital Essen, Essen, Germany

16 Department of Internal Medicine and Intensive Care Medicine, St. Antonius Hospital Eschweiler, Eschweiler, Germany

17 Department of Intensive Care Medicine, University Medical Center Hamburg-Eppendorf, Hamburg, Germany

18 Department of Cardiology and General Internal Medicine, Städtisches Klinikum Solingen gGmbH, Solingen, Germany

19 Department of Cardiology, Angiology and Pneumology, University of Heidelberg, Heidelberg, Germany

20 Department of Cardiovascular Surgery, Heinrich Heine University, Düsseldorf, Germany

21 Department of Internal Medicine, Medical Intensive Care Unit, University of Tuebingen, Tübingen, Germany

22 Department of Internal Medicine/Cardiology, Heart Center Leipzig, University Hospital, Leipzig, Germany

23 German Society of Medical Intensive Care and Emergency Medicine (Deutsche Gesellschaft für Internistische Intensivmedizin und Notfallmedizin, DGIIN), Berlin, Germany

24 German Society of Thoracic, Cardiac and Vascular Surgery (Deutsche Gesellschaft für Thorax-, Herz- und Gefäßchirurgie, DGTHG), Berlin, Germany

[25] German Society of Neuro-Intensive Care and Emergency Medicine (Deutsche Gesellschaft für Neurointensiv- und Notfallmedizin, DGNI), Jena, Germany

[26] German Interdisciplinary Association for Intensive Care and Emergency Medicine (Deutsche Interdisziplinäre Vereinigung für Intensiv- und Notfallmedizin, DIVI), Berlin, Germany

[27] German Society of Anaesthesiology and Intensive Care Medicine (Deutsche Gesellschaft für Anästhesiologie und Intensivmedizin, DGAI), Nürnberg, Germany

[28] German Resuscitation Council (GRC), Ulm, Germany

[29] German Cardiac Society (Deutsche Gesellschaft für Kardiologie, DGK), Düsseldorf, Germany

[30] German Society of Cardiotechnics (Deutsche Gesellschaft für Kardiotechnik, DGfK), Coswig, Saxony-Anhalt, Germany