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SYSTEMATIC REVIEW

Extracorporeal life support during cardiac arrest and cardiogenic shock: a systematic review and meta-analysis

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Abstract

Purpose: Veno-arterial extracorporeal life support (ECLS) is increasingly used in patients during cardiac arrest and cardiogenic shock, to support both cardiac and pulmonary function. We performed a systematic review and meta-analysis of cohort studies comparing mortality in patients treated with and without ECLS support in the setting of refractory cardiac arrest and cardiogenic shock complicating acute myocardial infarction.

Methods: We systematically searched MEDLINE, EMBASE, the Cochrane Central Register of Controlled Trials and the publisher subset of PubMed updated to December 2015. Thirteen studies were included of which nine included cardiac arrest patients ($n = 3098$) and four included patients with cardiogenic shock after acute myocardial infarction ($n = 235$). Data were pooled by a Mantel-Haenzel random effects model and heterogeneity was examined by the I^2 statistic.

Results: In cardiac arrest, the use of ECLS was associated with an absolute increase of 30 days survival of 13 % compared with patients in which ECLS was not used [95 % CI 6–20 %; $p < 0.001$; number needed to treat (NNT) 7.7] and a higher rate of favourable neurological outcome at 30 days (absolute risk difference 14 %; 95 % CI 7–20 %; $p < 0.0001$; NNT 7.1). Propensity matched analysis, including 5 studies and 438 patients (219 in both groups), showed similar results. In cardiogenic shock, ECLS showed a 33 % higher 30-day survival compared with IABP (95 % CI, 14–52 %; $p < 0.001$; NNT 13) but no difference when compared with TandemHeart/Impella (−3 %; 95 % CI −21 to 14 %; $p = 0.70$; NNH 33).

Conclusions: In cardiac arrest, the use of ECLS was associated with an increased survival rate as well as an increase in favourable neurological outcome. In the setting of cardiogenic shock there was an increased survival with ECLS compared with IABP.

Keywords: Extracorporeal membrane oxygenation, Extracorporeal life support, Acute myocardial infarction, Cardiac arrest, Cardiogenic shock, Cardiopulmonary resuscitation, Systematic review

Introduction

Veno-arterial extracorporeal life support (ECLS), also called extracorporeal membrane oxygenation (ECMO), is a modified form of cardiopulmonary bypass to support both cardiac and pulmonary function. Technological improvements and miniaturisation have made this technique more accessible and its use has increased over the past years, especially in patients with refractory cardiogenic shock or circulatory arrest [1, 2].

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Cardiogenic shock (CS) remains the leading cause of death in patients hospitalised for ST-segment elevation myocardial infarction (STEMI), as it may lead to multi-organ failure due to insufficient organ perfusion [3, 4]. In addition to pharmacological measures, treatment with mechanical circulatory support can be considered, especially in more severe forms of circulatory failure.

The aim of mechanical circulatory support in general is to support the failing heart and the overall circulation. Ideally, mechanical support is used as a bridge to either recovery or to other therapies such as a surgically implanted ventricular assist device (LVAD) or heart transplantation. It can be used in cardiogenic shock to prevent the development of multi-organ failure. In cardiac arrest patients, mechanical circulatory support enables treatment of the underlying cause while maintaining adequate perfusion.

A multitude of mechanical support devices have been developed over the past decades and this field is attracting increasing attention, especially after clinical trials did not show any clinical benefit for the intra-aortic balloon pump (IABP). Current European guidelines on cardiogenic shock no longer support routine IABP therapy, whereas short-term mechanical circulatory support holds a class IIb recommendation [5, 6].

Percutaneous cannulation techniques facilitate rapid insertion and initiation of ECLS therapy in emergency situations, such as cardiac arrest. Although ECLS usage has increased and several observational studies suggest that it has had a beneficial effect in both cardiac arrest and cardiogenic shock, no randomised controlled trials have been performed to date. Therefore, the actual evidence for its efficacy remains limited.

The main purpose of our study was to conduct a systematic review and meta-analysis of the available literature comparing ECLS with conventional therapy with regard to survival and neurological outcome in patients with cardiogenic shock after acute myocardial infarction (AMI) and patients with refractory cardiac arrest.

Methods

Selection criteria

Studies were considered for inclusion if they described outcome data from (A) patients with ECLS support and (B) a control group without ECLS support. Also, to qualify for inclusion, patients must have been diagnosed with either (1) refractory in-hospital or out-of-hospital cardiac arrest or (2) cardiogenic shock after AMI. Studies that did not report on survival to discharge, 30-day outcome or 6-month outcome were excluded. This meta-analysis was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) guidelines [7].

Search strategy

A medical librarian (J.L.) conducted a systematic search of OVID MEDLINE, OVID EMBASE, the Cochrane Central Register of Controlled Trials (CENTRAL) and the publisher subset of PubMed from inception to 7 December 2015. The search strategy consisted of controlled vocabulary (i.e. MeSH) and free text words for two basic concepts: (1) ECLS and (2) cardiogenic shock, cardiac arrest or myocardial infarction (see Appendix 1 in the electronic supplementary material for the entire MEDLINE search). Non-human studies, paediatric studies, case reports and reviews were excluded by double negation (NOT animals/NOT humans/) and/or excluding words in the title. We cross-checked the reference lists and the cited articles of the identified relevant papers for additional references. The bibliographic records retrieved were downloaded, imported and de-duplicated in ENDNOTE.

Data extraction and quality assessment

The retrieved articles were screened for relevance on title and abstract, followed by full-text screening by two independent investigators (D.O. and J.S.). In the event of overlapping patient cohorts the study with the longest follow-up period was included.

The prespecified patient and outcome data were independently extracted by two investigators (D.O. and J.S.). Differences between reviewers regarding study selection or data extraction were resolved by consensus. The quality of the studies was assessed using a modified version of the Newcastle-Ottawa Quality Assessment Scale for Cohort Studies [8].

Data analysis

The primary endpoint was 30-day survival. Secondary outcomes were long-term survival and 30-day and long-term favourable neurological outcome. Parameters describing the clinical course and complications were extracted, e.g. successful weaning from the cardiac assist device, bridging to destination therapy (long-term ventricular assist device or heart transplantation), timing of device placement, the occurrence of renal failure, stroke, peripheral vessel access complications and the need for blood transfusions (erythrocyte and fresh frozen plasma). If 30-day outcome data were not reported, in-hospital outcome data were used. For long-term data, the longest available follow-up was used. Neurological status was considered favourable when reported as either Pittsburgh Cerebral Performance Category (CPC) 1 or 2, or Modified Glasgow Outcome Score (MGOS) $\geq$4. Studies were grouped and presented by patient category: cardiac arrest or cardiogenic shock. A subcategory of propensity-matched studies is reported separately. Propensity score

matching is a method used to balance observed covariates in the two treatment arms by matching the propensity score which represents the probability of receiving ECLS therapy.

Results are presented as absolute risk differences with a 95 % confidence interval (CI) and a number needed to treat (NNT) or number needed to harm (NNH) and were combined by a Mantel-Haenzel random effects model. Heterogeneity across studies was examined by the I^2 statistic. Potential publication bias was assessed by visual assessment of constructed funnel plots. Tests were two-tailed and a p value of less than 0.05 was considered statistically significant. An I^2 of greater than 40 % was considered to be an indication of substantial heterogeneity. Review Manager (version 5.3) was used for statistical analysis.

Results

Search results

The de-duplicated results yielded a total of 1403 abstracts. A total of 59 relevant articles were identified and the full-text article was independently reviewed. Figure 1 shows a flowchart for selection of studies. One article was excluded as the intervention group contained both ECLS and IABP patients [9]. Fourteen articles were identified. Ten articles consisted of patients in refractory cardiac arrest [10–19]. However, two articles described the same cohort but with additional analysis [17 (Shin 2013 Int J Card)] [19 (Shin 2011 Crit Car Med]. This resulted in a total of 9 included cardiac arrest cohorts with a total of 3098 patients (708 ECLS versus 2390 control patients) (Table 1). Five of the cardiac arrest studies reported a propensity-matched analysis, including a total of 438 patients (219 in both groups) [10, 11, 13, 15, 19]. Four studies consisted of patients with cardiogenic shock with a total of 235 patients (151 ECLS versus 84 control patients) [20–23] (Table 1).

Quality of studies

As all studies were cohort studies and no randomised controlled trials were available, the quality of the studies was low with a high risk of bias (Appendix 2). However, funnel plots did not show skewed distributions, suggesting that no publication bias was involved (Appendix 3).

Cardiac arrest

Patient characteristics

Table 2 shows the baseline characteristics of the studies on ECLS in the setting of cardiac arrest. A total of nine studies were included with 3098 patients in total, 708 in the ECLS group and 2390 in the control group. All studies included cardiac arrest patients, although with different inclusion criteria such as in-hospital cardiac arrest (IHCA), out-of-hospital cardiac arrest (OHCA), witnessed or non-witnessed cardiac arrest and differing durations of cardiopulmonary resuscitation (CPR). Overall, ECLS patients were more likely to be younger, male, suffer from acute myocardial infarction and to undergo primary PCI.

Survival

Figure 2a shows 30-day survival of patients with refractory cardiac arrest. The usage of ECLS in this setting was associated with increased survival at 30 days (absolute risk difference 13 %; 95 % CI 6–20 %; $p < 0.001$; NNT 7.7). The long-term difference in survival was 15 % in favour of the ECLS treated patients (see supplementary file) (absolute difference 15 %; 95 % CI 11–20 %; $p < 0.0001$; NNT 6.7). Short-term outcome data displayed substantial heterogeneity ($I^2 = 64$ %), but long-term survival did not ($I^2 = 28$ %).

Neurological outcomes

Favourable neurological outcomes, defined as CPC score 1 or 2, are shown in Fig. 2b. The use of ECLS was associated with a higher rate of favourable neurological outcome at both 30 days (risk difference 14 %; 95 % CI 7–20 %; $p < 0.0001$; NNT 7.1) and during long-term follow-up (risk difference 11 %; 95 % CI 6–16 %; $p < 0.0001$; NNT 9.1) (supplementary data). Short-term outcome data were moderately heterogeneous ($I^2 = 52$ %) but the long-term survival data did not show substantial heterogeneity ($I^2 = 28$ %).

Other outcomes

Peripheral vessel complications were only reported by two studies. Blumenstein reported 17.3 % of patients with leg ischaemia or malperfusion in the ECLS arm and 2.9 % in the control arm. Maekawa et al. reported 7.7 % cannulation site infection, 15.4 % leg ischaemia requiring reperfusion and 2.9 % compartment syndrome in the ECLS patient group (supplementary data) [15]. Complication rates were very poorly reported. Only one of the cardiac arrest studies reported on renal failure (1.9 % in the ECLS patients versus 7 % in the control patients) [10]. Stroke and blood transfusions were not reported.

Propensity score matching

Five studies performed a propensity-matched analysis to balance observed covariates in the two treatment groups. The propensity score reflects the probability of receiving ECLS therapy. The baseline characteristics, after matching based on propensity score, can be seen in the supplementary data. The included patient population differed between studies in terms of location of the arrest (IHCA versus OHCA), witnessed or unwitnessed arrest,

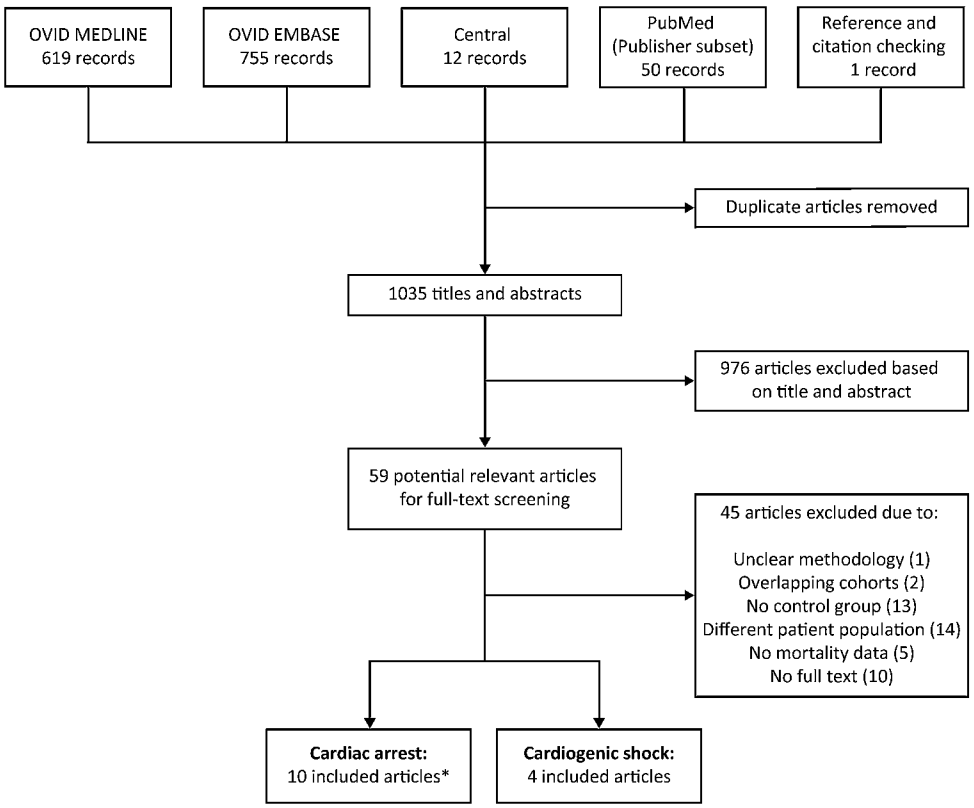

Fig. 1 Flowchart of the search strategy and selection of studies. *Asterisk*: 1 article reported on the same patient cohort as another included article, but provided additional data on propensity-matched analysis and was therefore included

Table 1 Summary of included cohort studies on cardiogenic shock and cardiac arrest patients

References	Country	Study period	Setting	Follow-up duration	Number of patients
Cardiac arrest					
Blumenstein et al. [10]	Germany	2009–2013	Retrospective, single centre	Long term[a]	353
Chen et al. [11]	Taiwan	2004–2006	Prospective, single centre	1 year	172
Chou et al. [12]	Taiwan	2006–2010	Retrospective, single centre	1 year	66
Kim et al. [13]	Korea	2006–2013	Prospective, single centre	3 months	499
Lee et al. [14]	Korea	2009–2014	Retrospective, single centre	In-hospital	955
Maekawa et al. [15]	Japan	2000–2004	Prospective, single centre	3 months	162
Sakamoto et al. [16]	Japan	2008–2011	Prospective, multi-centre	6 months	454
Shin et al. [17]	Korea	2003–2009	Retrospective, single centre	2 years	406
Siao et al. [18]	Taiwan	2011–2013	Retrospective, single centre	1 year	60
Cardiogenic shock					
Chamogeorgakis et al. [20]	USA	2006–2011	Retrospective, single centre	In-hospital	79
Lamarche et al. [21]	Canada	2000–2009	Retrospective, single centre	30 days	61
Sattler et al. [22]	Germany	2011–2012, 2012–2013	Retrospective, single centre	30 days	24
Sheu et al. [23]	Taiwan	1993–2002, 2002–2009	Prospective, single centre	30 days	71

[a] Not defined, median long-term follow-up was 1136 (823–1415) days

presumed cardiac origin and duration of CPR. After propensity matching, the patients treated with ECLS and control patients were comparable in terms of age and gender. There were more patients in the ECLS arm than in the control arm receiving primary PCI, as only one of the five propensity-matched studies included primary

Table 2 Baseline characteristics of the studies on ECLS-assisted cardiac arrest

References	Patient population	Criteria for ECLS allocation/ placement	Control arm	Number of patients (*n*)		Mean age (years)		Male (%)		Acute myocardial infarction (%)		Revascularisation (%)		CPR duration (min)		Interval between arrest and CPR	
				ECLS	Control	ECLS	Control	ECLS	Control	ECLS	Control	ECLS	Control	ECLS	Control	ECLS	Control
Blumenstein et al. [10]	Witnessed IHCA	ECLS was considered by the ECLS team if CPR >10 min and cardiac aetiology	Conventional CPR	52	272	72	75	54	61	29	21	–	–	33 (19–47)	20 (6–40)	–[d]	–[d]
Chen et al. [11]	Witnessed IHCA of cardiac origin, CPR >10 min	The decision was made by the attending doctors in charge. Exclusion for ECLS: failure to wean from bypass due to post-cardiotomy shock and patients who experienced shock requiring elective ECLS	Conventional CPR	59	113	57	60	85	65	63	71	44	6[a]	53 ± 37	43 ± 31	–[d]	–[d]
Chou et al. [12]	IHCA due to AMI, CPR >10 min	The decision to carry out ECPR is determined by the cardiovascular surgeon	Conventional CPR	43	23	61	70	93	74	100	100	100	43[a]	60 ± 34	49 ± 35	–[e]	–[e]

Table 2 continued

References	Patient population	Criteria for ECLS allocation/ placement	Control arm	Number of patients (*n*)		Mean age (years)		Male (%)		Acute myocardial infarction (%)		Revascularisation (%)		CPR duration (min)		Interval between arrest and CPR	
				ECLS	Control	ECLS	Control	ECLS	Control	ECLS	Control	ECLS	Control	ECLS	Control	ECLS	Control
Kim et al. [13]	Cardiac arrest patients with CPR (no trauma)	ECPR was indicated when presumed correctable cause of CA, witnessed arrest or presumed short no-flow time when unwitnessed arrest and informed consent of the family and in-hospital CPR >10 min	Conventional CPR	55	444	53	69	75	64	–	–	–	–	62 (47–89)	35 (21–50)	7 (0–13)	8 (5–12)
Lee et al. [14]	IHCA and OHCA CPR	Judgment of ECLS team. Only ECLS if CPR >10 min or repetitive arrest events without ROSC >20 min. No ECLS if unwitnessed OHCA or no bystander CPR	Conventional CPR	81	874	59	64	69	65	67	41	–	–	43 (21–60)	30 (15–48)	–	–
Maekawa et al. [15]	Witnessed OHCA of presumed cardiac origin, CPR >20 min	Initiation of ECPR was dependent on the attending physicians	Conventional CPR	53	109	54	71	83	73	–	–	40	6[b]	49 (41–59)	56 (47–66)	2 (0–8)	5 (0–9)

Table 2 continued

References	Patient population	Criteria for ECLS allocation/ placement	Control arm	Number of patients (*n*)		Mean age (years)		Male (%)		Acute myocardial infarction (%)		Revascularisation (%)		CPR duration (min)		Interval between arrest and CPR	
				ECLS	Control	ECLS	Control	ECLS	Control	ECLS	Control	ECLS	Control	ECLS	Control	ECLS	Control
Sakamoto et al. [16]	OHCA based on VF/VT, no ROSC >15 min after hospital arrival, <45 min between emergency call and hospital arrival; cardiac origin	Assignment of facility to ECPR or CPR group	Conventional CPR	260	194	56	58	90	89	64	59	38	11[b]	–	–	–	–
Shin et al. [17]	IHCA, witnessed, CPR >10 min	According to the discretion of the CPR team leader	Conventional CPR	85	321	60	62	62	63	45	26	41	7[a]	42 ± 26	41 ± 37	–[d]	–[d]
Siao et al. [18]	Cardiac arrest with initial VF (start CPR <5 min), no ROSC after 10 min CPR	Judgment of the attending physician	Conventional CPR	20	40	55	60	90	70	60	40	60	40[c]	70 ± 50	34 ± 18	–[f]	–[f]

Values are presented as mean ± standard deviation or as median (IQR)

CPR cardiopulmonary resuscitation, *PCI* percutaneous coronary intervention, *OHCA* out-of-hospital cardiac arrest, *IHCA* in-hospital cardiac arrest, *ROSC* return of spontaneous circulation, *AMI* acute myocardial infarction, *VF* ventricular fibrillation, *VT* ventricular tachycardia, *CA* cardiac arrest, *ECPR* ECLS-assisted cardiopulmonary resuscitation

[a] Reported as subsequent interventions (PCI or CABG)

[b] Reported as primary PCI

[c] Reported as subsequent interventions (PCI)

[d] Considered to be minimal as the inclusion criterion is (witnessed) IHCA

[e] IHCA so minimal no-flow time. In this study CPR duration was defined as time from collapse till ROSC, death or running of ECMO machine

[f] Not mentioned, but inclusion criteria state no-flow less than 5 min

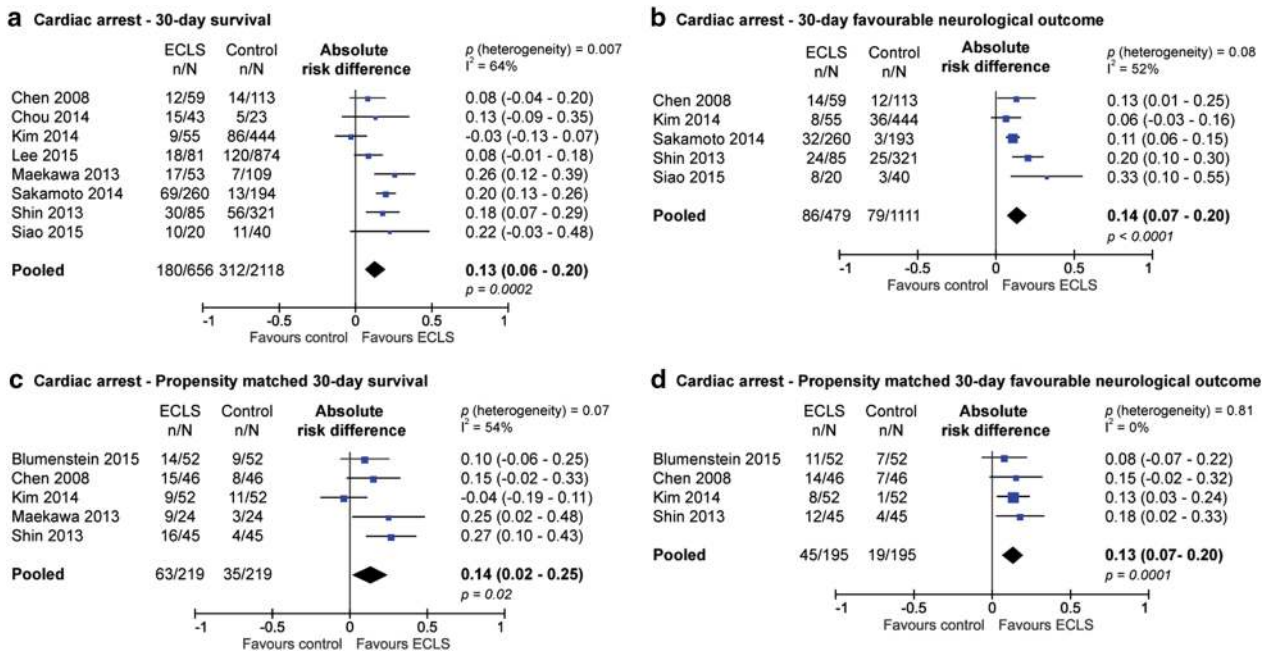

Fig. 2 Risk difference of 30-day survival (**a**) and favourable neurologic outcome (CPC 1 or 2) (**b**) and propensity-matched risk difference in 30-day survival (**c**) and favourable neurologic outcome (CPC 1 or 2) (**d**) in patients with cardiac arrest

PCI as a matching variable. The use of ECLS was associated with a higher survival rate at 30 days (difference 14 %; 95 % CI 2–25 %; $p = 0.02$; NNT 7.1) and in the long-term (difference 13 %; 95 % CI 6–20 %; $p = 0.001$; NNT 7.7) (Fig. 2c and supplementary data). Also, the use of ECLS was associated with a higher rate of favourable neurological outcome at both 30 days (risk difference 13 %; 95 % CI 7–20 %; $p = 0.0001$; NNT 7.7) and in the long-term (risk difference 14 %; 95 % CI 8–20 %; $p < 0.0001$; NNT 7.1) (Fig. 2d and supplementary data). In the propensity-matched analysis, short-term survival showed substantial heterogeneity ($I^2 = 54$ %), but long-term survival and the neurological outcomes showed no substantial heterogeneity ($I^2 = 0$ %).

Cardiogenic shock

Patient characteristics

Table 3 shows the baseline characteristics of the studies on ECLS in cardiogenic shock patients. A total of four studies were included with 235 patients in total, 151 in the ECLS group and 84 in the control group. All studies included cardiogenic shock patients after myocardial infarction, albeit with different inclusion criteria such as refractory CS, progressive CS or decompensated cardiomyopathy. In two studies, the control arm consisted of IABP support, and in two other studies, the control arm consisted of patients supported by Impella 5.0, Impella RD or TandemHeart. Patients in the ECLS arm were generally younger and were less likely to suffer from acute myocardial infarction (Table 3). In the two studies with IABP support in the control group, all patients were diagnosed with STEMI and treated with primary PCI.

Survival outcomes

Figure 3 shows the absolute number of survivors among patients with and without ECLS treatment, with the absolute risk difference for each study, stratified by the different control arms. The studies with IABP in the control arm showed that ECLS support in the setting of cardiogenic shock was associated with improved 30-day survival (risk difference 33 %; 95 % CI 14–52 %; $p = 0.0008$; NNT 3). When ECLS was compared with Impella or TandemHeart, ECLS was not associated with a significant difference in 30-day survival (risk difference −3 %; 95 % CI −21 to 14 %; $p = 0.70$; NNH 33). When combining the control groups (IABP and Impella/TandemHeart), the use of ECLS was not associated with a change in 30-day survival in patients with cardiogenic shock (risk difference 14 %, 95 % CI -8-35 %; $p = 0.20$; NNT 7.1). The analysis stratified according to control arm did not show any heterogeneity ($I^2 = 0$ %), but the overall effects were substantially heterogeneous ($I^2 = 60$ %). The long-term survival and neurological outcomes were not described in these studies.

Table 3 Baseline characteristics of the studies on ECLS in cardiogenic shock patients

References	Patient population	Criteria for ECLS allocation/placement	Control arm	Number of patients (*n*)		Mean age (years)		Male (%)		Acute myocardial infarction (%)		Primary PCI (%)	
				ECLS	Control	ECLS	Control	ECLS	Control	ECLS	Control	ECLS	Control
Chamogeorgakis et al. [20]	Post/infarction or decompensated cardiomyopathy (ischaemic or non-ischaemic) cardiogenic shock	Patients receiving heart compressions, ECLS is the only option. For more stable patients, TandemHeart or Impella. For isolated right ventricular failure, TandemHeart is favoured. In left ventricular failure, Impella 5.0 or TandemHeart can be used	Impella 5.0/TandemHeart[a]	61	18	53	58	80	72	53	78	–	–
Lamarche et al. [21]	Acute, refractory, cardiogenic shock with potential for recovery and systemic perfusion did not improve with IABP and inotropes	Biventricular failure and oxygenation problems: ECLS. Unilateral failure: Impella	Impella 5.0/Impella RD	32	29	50	54	63	83	41	38	–	–
Sattler et al. [22]	Progressive cardiogenic shock due to acute myocardial ischaemia, and successful PCI	Enrolment during period with ECLS availability and ECLS is technically feasible	IABP	12	12	55	68	83	83	100	100	100	100
Sheu et al. [23]	STEMI with primary PCI and profound cardiogenic shock[b]	Enrolment date in period with ECLS availability	IABP	46	25	65	67	–	–	100	100	100	100

CPR cardiopulmonary resuscitation, *PCI* percutaneous coronary intervention, *AMI* acute myocardial infarction, *VF* ventricular fibrillation, *VT* ventricular tachycardia, *CA* cardiac arrest, *ECPR* ECLS-assisted cardiopulmonary resuscitation

[a] 7 Impella, 11 TandemHeart

[b] Profound shock: systolic blood pressure <75 mmHg despite inotropic agents and IABP

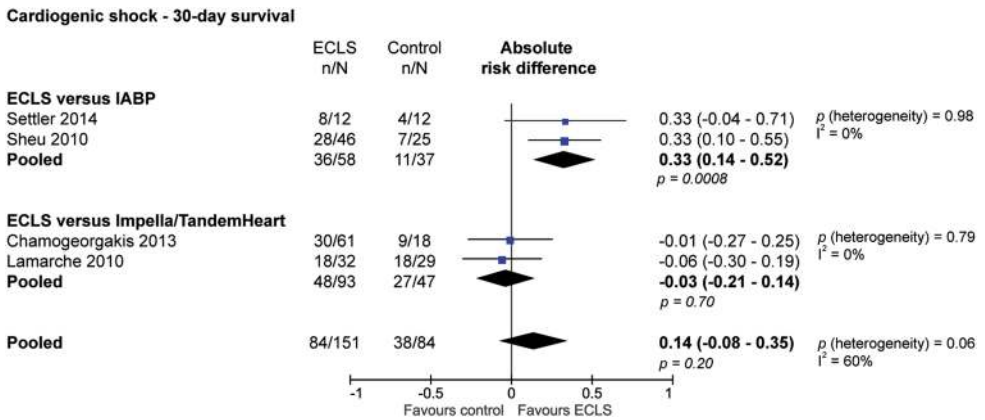

Fig. 3 Difference of 30-day survival of patients with cardiogenic shock, stratified according to different control therapies (IABP or Impella/TandemHeart)

Other outcomes

The percentage of patients who were successfully weaned from ECLS and the percentage of patients who were bridged to long-term ventricular assist device or heart transplant are shown in the supplementary data. Only Sattler et al. reported the time of device placement: in one patient, ECLS was placed before PCI, in nine patients immediately after PCI and in two patients ECLS therapy was initiated within 24–48 h after PCI with IABP support. Peripheral vessel complications and blood transfusions are shown in the supplementary data. Only one study reported the incidence of renal failure, with renal failure occurring in 58.3 % of patients treated with ECLS and in 25.0 % of the control patients [22]. Stroke was not reported by any study.

Discussion

We conducted two meta-analyses of cohort studies comparing ECLS therapy with varying control groups in the settings of cardiac arrest and cardiogenic shock. In the setting of cardiac arrest, the usage of ECLS showed an increase in survival of 13 % and an increase of favourable neurological outcome of 14 % at 30-days compared with no usage of ECLS. This effect was still prominent after baseline characteristics were adjusted by propensity matching. In patients with cardiogenic shock, ECLS was associated with higher 30-day survival compared with IABP, but there was no difference in survival when compared with Impella or TandemHeart.

In the absence of randomised controlled trials, we included non-randomised studies and therefore cannot rule out the influence of confounders. As a result, there was a difference in baseline characteristics between ECLS and control patients. ECLS-treated patients were more likely to be male, younger, suffer from acute myocardial infarction and were more likely to undergo primary PCI—all factors known to be associated with increased survival in this setting [24–26]. Another potentially important bias towards poor outcomes in the 'control/no-ECLS' group may be due to the fact that sicker patients may have been considered too ill to benefit from ECLS therapy and others may have died before they could receive ECLS therapy. As it is difficult to reliably distinguish between the effect of ECLS therapy and the effect of the bias and confounding inherent to cohort studies, the results of this analysis should be interpreted with caution. Nevertheless, the propensity-matched analysis in cardiac arrest, with matching baseline characteristics, showed results comparable with the outcome of the cohort studies.

In addition to the difference in baseline characteristics of the patients, differences in the treatment of patients might have influenced the results. Patients with cardiac arrest treated with ECLS were more likely to be revascularised. This finding suggests that the use of ECLS allows for more frequent revascularisation. Kagawa et al. investigated the effectiveness of intra-arrest PCI during ECLS, and they reported a higher survival rate in the intra-arrest PCI groups compared with delayed PCI (36 versus 12 %) [27]. The fact that ECLS-assisted CPR allowed for timely treatment of the underlying cause, such as intra-arrest PCI, might partly explain the increased survival in ECLS-assisted CPR.

In the cardiogenic shock patients, the difference in treatment effect may be explained by the amount of haemodynamic support that is generated by the mechanical support device. The used Impella devices (5.0 and RP) and TandemHeart actively support the circulation with around 4 L/min, which is comparable to ECLS, whereas the IABP only passively supports the overall circulation with ca. 0.5 L/min. However, a small meta-analysis of randomised trials comparing IABP ($n = 47$)

with Impella/TandemHeart ($n = 53$) in CS complicating AMI did not show any difference in outcome [28]. This seems to contradict the previous hypothesis that ECLS, TandemHeart and Impella 5.0 might all be superior to IABP as they provide more haemodynamic support. This apparent contradiction may be explained by the different characteristics of the patients included, the differences in definition of (profound) CS and the low number of patients included in both meta-analyses. Although the support level of the used devices may be similar (around 4 L/min), they have different specifications and therefore different clinical indications [4, 5].

The variety of inclusion criteria in the included studies is likely to have contributed to the heterogeneity. Although we aimed to include patients with acute myocardial infarction, some cardiogenic shock studies included patients with a wide variety of aetiologies (100 % AMI in the IABP studies, but lower in the Impella/Tandemheart studies (no exact number reported)). In the cardiac arrest studies, there was variation in the location of the arrest, duration of no-flow and CPR. The inclusion criteria resulted in relatively low no-flow times as most studies included IHCA arrest, witnessed OHCA with bystander CPR, or mandatory low no-flow times. It is not known whether shorter no-flow and CPR duration before deploying ECLS results in a better outcome compared with conventional CPR. However, survival and outcome deteriorate as duration of no-flow and CPR increases [11].

Although vascular and bleeding complications are known to occur frequently during ECLS therapy, only a few of the included studies reported on these complications. Two previously published pooled analyses of complications of ECLS both reported high complication rates [29, 30]. They did not compare those rates with non-ECLS-treated patients. In these pooled analyses, lower limb ischaemia occurred in 16.9 and 10.7 %, which is comparable with our range of peripheral vessel complications, which is between 8.7 and 25 %. The occurrence of events may be directly related to ECLS therapy, or indirectly to the critical conditions of patients treated with ECLS. Either way we must keep in mind that survival with good neurological outcome might outweigh the risk for complications. In addition, complications during ECLS can only occur when patients are still alive for complications to occur. Therefore, the value of complications in these extremely high-risk patients is a relative one. The current meta-analysis found a survival rate of 45.2 % in cardiogenic shock patients and 27.4 % in the cardiac arrest patients treated with ECLS. These numbers are consistent with data from Xie et al., who performed a pooled analysis of observational cohort studies (without control arm) on patients treated with ECLS for refractory cardiogenic shock ($n = 659$) or for cardiac arrest ($n = 277$), and demonstrated a 30-day survival of 52.5 % in CS and 36.2 % in cardiac arrest [31].

Currently, ECLS has a class IIb recommendation (may be considered) in the European and American guidelines on myocardial revascularisation [6, 32]. The European Resuscitation Council (ERC) guidelines recommend that ECLS-assisted CPR should be considered to facilitate interventions [33]. Although the guidelines recommend consideration of ECLS, ECLS requires multidisciplinary expertise, which is often only available in a limited number of specialised centres. Experience is gained by providing ECLS support in remote locations and in the prehospital field to allow transfer to an experienced ECLS centre [27, 34–36]. In addition, the high cost of ECLS is a limiting factor, which mandates appropriate case selection.

Although the findings of this meta-analysis were limited by the heterogeneity of included studies, in the absence of large randomised trials, this pooled analysis represents the best available method for evaluating ECLS. These data should be taken into account when updating the clinical guidelines on cardiac arrest. Ultimately, to clarify the role of ECLS in cardiogenic shock and cardiac arrest, a randomised controlled trial should be undertaken; however, many randomised trials in this patient category have been aborted as a result to low inclusion rates [37]. Therefore, while aiming for a randomised trial, large multicentre registries could be the first step towards identifying patients that may benefit from ECLS or other circulatory support devices.

In conclusion, the current meta-analysis aggregated all available evidence on the effectiveness of ECLS in the continuous field of cardiac failure, ranging from cardiogenic shock to cardiac arrest. In the setting of refractory cardiac arrest, the meta-analysis showed increased survival and favourable neurological outcomes in the ECLS-treated patients. In the setting of cardiogenic shock there was an increased survival with ECLS compared with IABP.

Electronic supplementary material

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Compliance with ethical standards

Conflicts of interest

J.P.S. Henriques reports research grants outside the submitted work. The other authors do not declare any conflicts of interest.

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