Interventional procedure overview of venoarterial extracorporeal membrane oxygenation (VA ECMO) for acute heart failure

Contents

Table 1 Abbreviations

Abbreviation	Definition
ADHF	Acute decompensated heart failure
AMI	Acute myocardial infarction
BP	Blood pressure
CABG	Coronary-artery bypass grafting
CI	Confidence interval
CNS	Central nervous system
CPC	Cerebral Performance Category
CPR	Cardiopulmonary resuscitation
CS	Cardiogenic shock
CV	Cardiovascular
dMCS	Durable mechanical circulatory support
ECLS	Extracorporeal life support
ECPR	Extracorporeal cardiopulmonary resuscitation
EEG	Electroencephalogram
ELSO	Extracorporeal Life Support Organization
HF	Heart failure
HR	Hazard ratio
HRQoL	Health related quality of life
HTx	Heart Transplant
IABP	Intra-aortic balloon pump
ICU	Intensive care unit
IHCA	In hospital cardiac arrest
INTERMACS	Interagency Registry for Mechanically Assisted Circulatory Support
IP-1	INTERMACS profile 1
IQR	Interquartile range
ITT	Intention to treat
LV	Left ventricular
LVAD	Left ventricular assist device
LVEF	Left ventricular ejection fraction
MAP	Mean arterial pressure
MCS	Mechanical circulatory device
MI	Myocardial infarction
NSTEMI	Non-ST-elevation myocardial infarction
OHCA	out of hospital cardiac arrest

PCI	Percutaneous coronary intervention
RR	Relative risk
SCAI	Society for cardiovascular angiography and interventions
SD	Standard deviation
STEMI	ST-elevation myocardial infarction
VA ECMO	Venoarterial extracorporeal membrane oxygenation
VAD	ventricular assist device
VTE	Venous thromboembolism

The condition, current practice, unmet need and procedure

Information about the procedure, condition, current practice and unmet need is available in section 2 and 3 of NICE's interventional procedures consultation document on VA ECMO for severe acute heart failure in adults.

Clinical assessment tools

Some studies assessed people with acute heart failure using assessment tools:

- INTERMACS profile (IP): this is a 7-profile categorisation for people with advanced heart failure, ranging from IP-1 as the most critical, to IP-7 as the least critical. IP-1 (critical cardiogenic shock), IP-2 (progressive decline on inotropes), IP-3 (stable but inotrope dependent), IP-4 (resting symptoms on oral therapy at home), IP-5 (exertion intolerant), IP-6 (exertion limited), IP-7 (placeholder – living comfortably with meaningful activity limited to mild physical exertion).
- Society for Cardiovascular Angiography and Interventions (SCAI) SHOCK classification: this is a 5-category classification (A to E) that indicate the severity of cardiogenic shock. A (haemodynamically stable patient not experiencing symptoms of CS, but at risk for its development), B (clinical evidence of haemodynamic instability without evidence of hypoperfusion), C

(clinical evidence of hypoperfusion that requires pharmacologic or mechanical support), D (clinical evidence of shock that worsens or fails to improve despite therapy escalation), E (refractory shock or actual/impending circulatory collapse).

Outcome measures

The main outcomes included survival or mortality. Some studies evaluated neurological outcomes. The measures used are detailed in the following paragraphs.

- Cerebral performance categories (CPC): this is a 5-category measure used to assess neurological outcome. Categories 1 (good cerebral performance: conscious, alert, capable of normal life) and 2 (moderate cerebral disability: conscious, alert, sufficient cerebral function for activities of daily life) are considered to show a good neurological outcome. Categories 3 (severe cerebral disability), 4 (coma/vegetative state) and 5 (certified brain death) are considered to be a poor neurological outcome.

Evidence summary

Population and studies description

This interventional procedure overview is focused on acute HF. Two additional overviews have been developed focusing on VA ECMO in post cardiotomy and as extracorporeal cardiopulmonary resuscitation (ECPR). Some of the evidence includes a mix of indications and has been presented in more than one overview.

This overview is based on approximately 32,000 people from 4 systematic reviews (Elsaeidy 2024, Sohail 2022, Alba 2021, Vishram-Nielsen 2023), 3 randomised controlled trials (Thiele 2023, Banning 2023, Ostadal 2023), 1 retrospective registry study (Olson 2020) and 1 single centre retrospective

study (Cheng 2019). The 3 randomised controlled trials (Thiele 2023, Banning 2023, Ostadal 2023) were also included in the Elsaeidy 2024 systematic review. There were 15 overlaps accounting for 11,766 people in primary studies included across 3 systematic reviews (Sohail 2022, Alba 2021, Vishram-Nielsen 2023). This is a rapid review of the literature, and a flow chart of the complete selection process is shown in figure 1. This overview presents 9 studies as the key evidence in table 2 and table 3, and lists 30 other relevant studies in appendix B, table 5.

All randomised controlled trials included in the key evidence, and those included in the systematic review by Elsaeidy (2024), were conducted in Europe (Thiele 2023, Banning 2023, Ostadal 2023). The 3 systematic reviews of observational studies included in the key evidence included studies from Asia, Australia, Europe, North America and South America (Sohail 2022, Alba 2021, Vishram-Nielsen 2023). The included registry study used data from the Extracorporeal Life Support Organization (ELSO) which collates data worldwide (Olson 2020). The single centre retrospective study was conducted in the US (Cheng 2019).

Most key evidence studies included people with cardiogenic shock (CS). Of the key studies including people with CS, 2 systematic reviews and 2 randomised controlled trials specifically included people with CS complicating acute myocardial infarction (AMI) (Sohail 2022, Elsaeidy 2024, Banning 2023, Thiele 2023). 1 systematic review included people receiving VA ECMO for fulminant myocarditis (Vishram-Nielsen 2023), and 1 registry study included people receiving VA ECMO for peripartum cardiomyopathy (Olson 2020).

The systematic review by Elsaeidy (2024) included 4 randomised controlled trials including 611 people. Three of these are reported separately in the key evidence (Thiele 2023, Banning 2023, Ostadal 2023), the other study being a pilot study preceding the randomised controlled trial by Ostadal (2023). Half of the studies

were deemed to have an overall low risk of bias, and 2 had some concerns of bias overall about deviations from the intended intervention and outcome measurement (Thiele 2023) and about the selection of the reported results (Ostadal 2023). The comparator in all trials was standard medical therapy, however 1 trial also allowed later cross-over of patients to VA ECMO if they continued to be haemodynamically unstable. The mean age of people included in the studies ranged from 60 to 68 years, and the proportion of males ranged from 73 to 95%. All studies reported outcomes at 30 days and 2 studies reported outcomes at 1 year follow-up.

The randomised controlled trial reported by Thiele (2023), which was also included in the Elsaeidy (2024) systematic review, compared VA ECMO to standard medical therapy alone in 417 adults with CS complicating AMI. Two thirds of people included presented with ST-segment elevation myocardial infarction (STEMI). All trial participants received early revascularisation ahead of the intervention. Intraaortic balloon pump (IABP) was permitted as an escalation therapy, and although the trial protocol forbade any cross-over, VA ECMO was initiated in 26 people in the control group (12.5%). The median age was 62 years and 81% of the population were male. Trial outcomes were reported at 30 days.

The randomised controlled trial reported by Banning (2023), which was also included in the Elsaeidy (2024) systematic review, compared early peripheral VA ECMO to standard medical therapy alone in 35 adults with CS complicating AMI. Due to the impact of the COVID-19 pandemic, the trial was stopped before completion of recruitment. The median age was 67 years and 81% of the population were male. Trial outcomes were reported at 30 days and 1 year follow-up.

The randomised controlled trial reported by Ostadal (2023), which was also included in the Elsaeidy (2024) systematic review, compared immediate VA

ECMO to early conservative therapy in 117 adults with rapidly deteriorating or severe CS. The most common cause of CS in both arms was STEMI (50%) followed by decompensation of chronic heart failure (23%). The study permitted cross-over from the control group, to receive VA ECMO in the case of worsening haemodynamic stability. 39% of the control group required downstream VA ECMO therapy. The median age was 67 years and 74% of the population were male. Trial outcomes were reported at 30 days.

The systematic review by Sohail (2022) included 72 observational studies reporting on 10,276 adults who had VA ECMO for CS complicating AMI. The median concomitant IABP use across the included studies was 70%. The median age was 60 years and 78% of the population were male. Meta-analyses of the studies pooled short-term outcomes from studies with follow-ups of 7 days, 30 days and hospital discharge.

The systematic review by Alba (2021) included 306 observational studies reporting on 29,289 people with CS of any aetiology. The largest number of studies reported on people with CS after cardiac arrest (ECPR), CS complicating AMI, and postcardiotomy cardiogenic shock. Risk of bias across studies was considered low in 219 (72%), moderate in 81 (26%), and high in 6 (2%) studies. The age of people included in the studies ranged from 47 to 61 years, and 22% to 59% of the population were female. Meta-analyses of the studies pooled short-term outcomes from studies with follow-ups of 30 days and hospital discharge.

The single-centre retrospective study conducted in the US by Cheng (2019) included 149 people who survived VA ECMO (n=118) or CentriMag VAD (n=31) support as a bridge to recovery. The most common indication for ECMO intervention was postcardiotomy CS (36%), followed by allograft failure (27%), AMI (24%) and acute decompensated heart failure (ADHF) (14%). The median

age was 59 years and 68% of the population were male. The median follow-up time was 306 days (IQR: 59 to 916 days).

The systematic review by Vishram-Nielsen (2023) included 54 observational studies reporting on 2,388 people with fulminant myocarditis. The median age was 41 years and 50% of the population were male. Meta-analyses of the studies pooled short-term outcomes from studies with follow-ups of 30 days and hospital discharge.

The retrospective ELSO registry study by Olson (2020) reported outcomes for people with peripartum cardiomyopathy treated with VA ECMO. The median age was 31 years and 42% were of white ethnicity. Outcomes were reported for follow-up period until hospital discharge.

Table 2 presents study details.

Figure 1 Flow chart of study selection

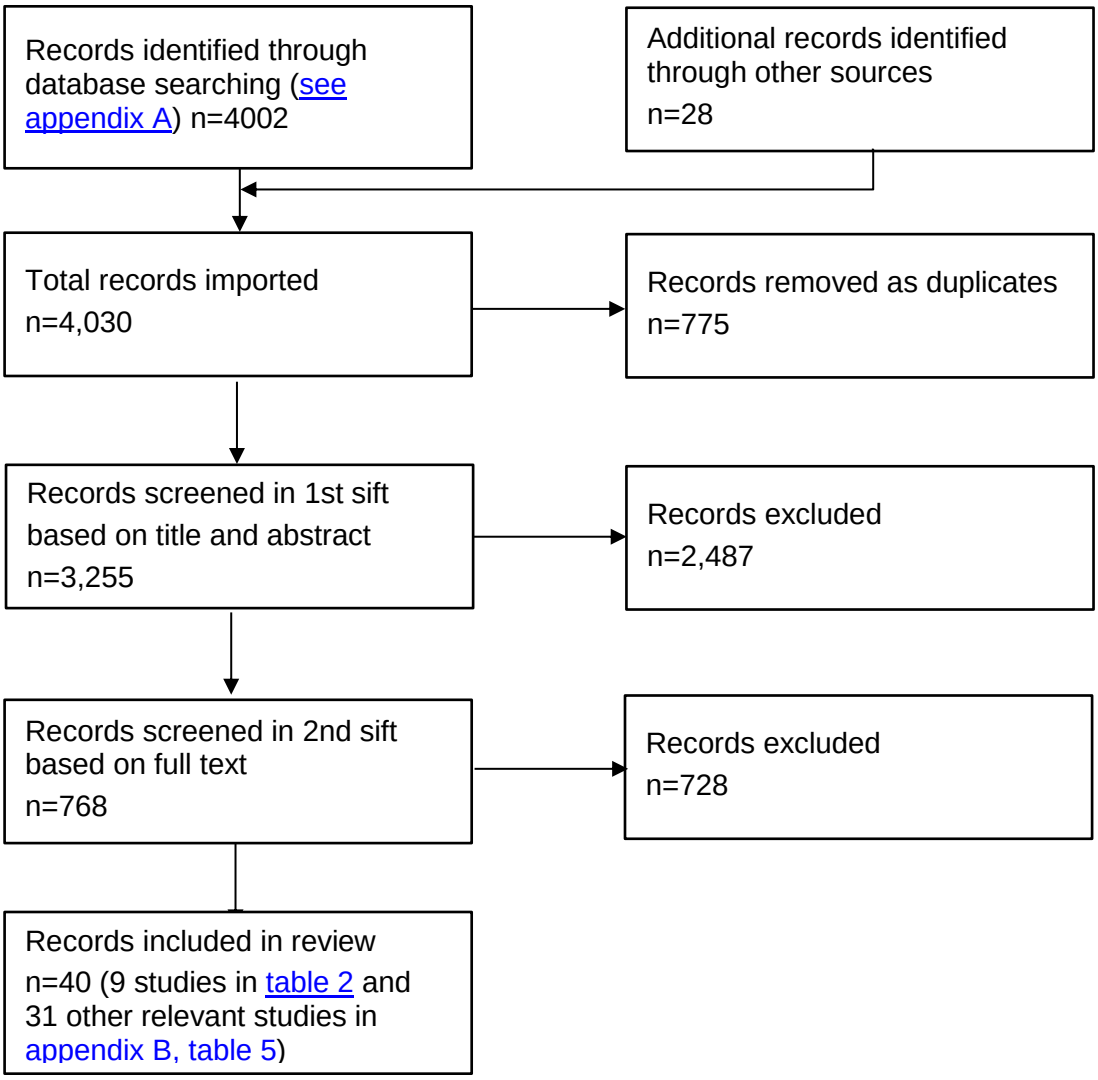

Table 2 Study details

Study no.	First author, date country	Characteristics of people in the study (as reported by the study)	Study design	Inclusion criteria	Intervention	Follow up
1	Elsaeidy, 2024 Belgium, Czech Republic, Germany, Latvia, Norway, Slovenia Spain, UK	**n=611** Mean age ranged from 60 to 68 years Males: 80% (range 73% to 95%) Type of MI: STEMI (range 0 to 61.9%) NSTEMI (range 6.7% to 61.9%)	Systematic review and meta-analysis of 4 RCTs (Banning, 2023; Thiele, 2023; Ostadal, 2023, Lackermair, 2021) Search date: Sept 2023 All open label RCTs	RCTs that investigate the efficacy and safety of ECMO compared to standard care in managing **CS-complicating AMI** patients.	• Intervention: immediate VA ECMO • Comparator: usual medical therapy alone	30 days (4 studies) 1 year (2 studies)

Study no.	First author, date country	Characteristics of people in the study (as reported by the study)	Study design	Inclusion criteria	Intervention	Follow up
2	Thiele, 2023, Germany, Slovenia ELCS-SHOCK	**n=417** (ECLS n=209) Median age (years) • Standard=63 • ECLS=62 Male (%) • Standard=81.2 • ECLS=81.3 Median LVEF on admission • Standard=30% • ECLS=30% Two thirds of patients presented with ST-segment elevation myocardial infarction. 77.7% patients underwent CPR before randomisation. PCI was performed in 96.6% patients.	Randomised controlled trial, open label. Randomisation was done by means of a web-based system with the use of randomly changing blocks and stratification according to the trial site.	Patients aged between 18 and 80 with **CS-complicating AMI** and planned early revascularisation by either PCI or coronary-artery bypass grafting (CABG) CS defined as stage C, D, or E of the SCAI criteria. Excluded were people who had undergone CPR for more than 45 minutes before randomisation or who had a mechanical cause of CS or severe peripheral-artery disease precluding the insertion of cannulae.	• Intervention: ECLS plus usual medical therapy • Comparator: usual medical therapy alone ECLS was not initiated in 17 patients in the ECLS group (8.1%), including in 4 patients who died before initiation. ECLS was initiated in 26 patients in the control group (12.5%), including 22 patients within 24 hours after randomisation and 4 patients thereafter. IABP was permitted as escalation therapy for the control group.	30 days

Study no.	First author, date country	Characteristics of people in the study (as reported by the study)	Study design	Inclusion criteria	Intervention	Follow up
3	Banning, 2023, Belgium, Germany, Latvia, Norway, Spain, UK EURO SHOCK	**n=35** (VA ECMO n=17) Median age (years) • Standard=67 • ECMO=68 Male (%) • Standard=89% • ECMO=81% Median LVEF on admission • Standard=25% • ECMO=20%	Randomised controlled trial, open label. Randomisation was carried out using a web-based randomisation system stratified by out-of-hospital cardiac arrest (OHCA). Due to the impact of the COVID-19 pandemic, the trial was stopped before completion of recruitment.	People presenting with **CS-complicating AMI** and who had had attempted/ successful primary PCI (PPCI) of the culprit lesion were enrolled if there was persistent CS 30 mins after the procedure. CS defined as BP <90 mmHg or maintained above 90 mmHg with the addition of vasopressor or inotropic support, with evidence of hypoperfusion.	• Intervention: Immediate PCI + early peripheral VA ECMO and standard care (pharmacological support). • Comparator: Immediate PCI + standard care (pharmacological support). IABP was permitted as escalation therapy for the control group, or for left ventricular unloading in the VA ECMO group. 5 patients randomised to ECMO did not receive ECMO.	30 days, 1 year
4	Ostadal, 2023 Czech Republic	**n=117** (ECMO n=58) Median age (years)	Randomised controlled trial, open label.	People over 18 with **rapidly deteriorating or severe CS**.	• Intervention: Immediate VA ECMO	30 days

Study no.	First author, date country	Characteristics of people in the study (as reported by the study)	Study design	Inclusion criteria	Intervention	Follow up
	ECMO-CS	• Standard= 65 (58 to 71) • ECMO= 67 (60 to 74) Male (%) • Standard= 72.9 • ECMO= 74.1 The most common cause of CS in both arms was STEMI (50.4%) followed by decompensation of chronic heart failure (23.1%).	An automated, web-based system was used for randomisation with permuted blocks, with stratification according to the type of cardiogenic shock (rapidly deteriorating or severe), and the trial centre.	Rapidly deteriorating CS defined as SCAI stage D to E Severe CS defined as SCAI stage D	• Comparator: early conservative therapy • 39% of the conservative therapy group required downstream "bailout" VA ECMO therapy in case of hemodynamic worsening.	
5	Sohail, 2022, Asia, Australia, Europe, North America	**n=10,276** Median age (years)=60 (IQR 56.35 to 63.94) Male % = 78%	Systematic review and meta-analysis of 72 studies. Search date: August 2020	Adults (over 18 years) receiving VA ECMO for **CS complicating AMI**.	• Intervention: VA ECMO • Median concomitant IABP use = 70% (IQR 35.1 to 86)	Short term mortality (7, 30 days, discharge)

Study no.	First author, date country	Characteristics of people in the study (as reported by the study)	Study design	Inclusion criteria	Intervention	Follow up
6	Alba, 2021 Europe, Asia, North America, South America, Australia	**n=29,289** Age (years): Range 47 to 61 Female %: Range 22 to 59 <u>Indication</u> • ECPR: 7,814 (113 cohorts) • Post-AMI: 7,774 (80 cohorts) • Postcardiotomy: 8,231 (64 cohorts) • Post-HTx: 771 (25 cohorts) • Heart failure: 3,567 (33 cohorts) • Myocarditis: 906 (13 cohorts) • Pulmonary embolism: 221 (10 cohorts)	Systematic review and meta-analysis of 306 observational studies. Search date: June 2019	Adults (aged 18 and over) with **CS of any aetiology**, with VA ECMO implantation.	• Intervention: VA ECMO • Concomitant IABP: Range 20 to 67%	30 day or discharge

Study no.	First author, date country	Characteristics of people in the study (as reported by the study)	Study design	Inclusion criteria	Intervention	Follow up
7	Cheng, 2019 US	**n=149** (ECMO n=118) Median age (years)=59 (51-67) Male=67.8% Aetiology: • AMI: 24.2% • Acute decompensated HF: 14.4% • Postcardiotomy CS: 35.6% • Allograft failure: 26.8%	Single centre retrospective study (26-bed ICU) Search date: 2010 to 2016	People who survived VA ECMO or CentriMag VAD support as a short-term MCS as **bridge to recovery**.	• Intervention: VA ECMO (n=118)	Median 306 days (IQR 58.925 to 916.75)
8	Vishram-Nielsen, 2023 Asia, Australia, Europe, North America	**n=2,388** Median age (years) = 41 (IQR 37 to 47) Male % = 50%	Systematic review and meta-analysis of 54 retrospective studies. Search date: July 2020	Adult (aged 18 and over) patients with **fulminant myocarditis**, evaluating short-term mortality after VA ECMO implantation.	• Intervention: VA ECMO	30 day, hospital discharge

Study no.	First author, date country	Characteristics of people in the study (as reported by the study)	Study design	Inclusion criteria	Intervention	Follow up
9	Olson, 2020 Worldwide	**n=88** Median age (years): 31.1 (IQR 25.4 to 35.2)	Retrospective ELSO registry study Search date: 2007 to 2019	People with **peripartum cardiomyopathy** treated with ECMO.	• Intervention: VA ECMO	Hospital discharge

Table 3 Study outcomes

First author, date	Efficacy outcomes	Safety outcomes
Elsaeidy, 2024	**Pooled 30-day mortality (4 trials)** • VA ECMO: 45.9% (140/305) • Control: 48.4% (148/306) RR 0.95, 95% CI: 0.80 to 1.12; p=0.54, I^2=0% **Pooled 30-day reinfarction (3 trials)** • VA ECMO: 1.6% (4/244) • Control: 2.0% (5/247) RR 0.87, 95% CI: 0.25 to 3.04; p=0.83, I^2=0%	**Pooled bleeding events (4 trials)** • VA ECMO: 25.2% (76/302) • Control: 11.8% (36/306) RR 2.14, 95% CI: 1.49 to 3.07; p<0.0001, I^2=0% **Pooled acute kidney injury/RRT (3 trials)** • VA ECMO: 8.9% (25/281) • Control: 14.0% (40/285) RR 0.65, 95% CI: 0.41 to 1.04; p=0.07, I^2=0% **Pooled stroke (4 trials)** • VA ECMO: 4.0% (12/302) • Control: 3.6% (11/306) RR 1.14, 95% CI: 0.52 to 2.49; p=0.75, I^2=18%

First author, date	Efficacy outcomes	Safety outcomes
		Pooled sepsis (4 trials) • VA ECMO: 17.7% (54/305) • Control: 16.7% (51/306) RR 1.07, 95% CI: 0.77 to 1.48; p=0.85, I^2=0% **Pooled pneumonia (2 trials)** • VA ECMO: 24.0% (18/75) • Control: 24.7% (19/77) RR 0.97, 95% CI: 0.57 to 1.65; p=0.90, I^2=0%
Thiele, 2023 ECLS-SHOCK	**Death from any cause at 30 days** • ECLS: 47.8% (100/209) • Control: 49.0% (102/208) RR 0.98, 95% CI: 0.80 to 1.19; p=0.81 **Myocardial reinfarction** • ECLS: 1% (2/209) • Control: 1% (2/208) RR 1.00, 95% CI: 0.07 to 12.72 **Rehospitalisation for congestive heart failure within 30 days** • ECLS: 1.4% (3/209) • Control: 1% (2/208) RR 1.49, 95% CI: 0.24 to 13.61 **Subgroup analysis death from any cause 30 days by age** <u>≤65 years</u> • ECLS: 40.3% (50/124) • Control: 36.6% (41/112)	**Moderate or severe bleeding:** • ECLS: 23.4% (49/209) • Control: 9.6% (20/208) RR 2.44, 95% CI: 1.50 to 3.95. **Poor neurological outcome (CPC 3 or 4)** • ECLS: 24.8% (27/109) • Control: 22.6% (24/106) RR 1.03, 95% CI: 0.88 to 1.19 **Peripheral ischaemic vascular complications warranting surgical or interventional therapy** • ECLS: 11% (23/209) • Control: 3.8% (8/208) RR 2.86, 95% CI: 1.31 to 6.25. **Renal replacement therapy** • ECLS: 8.1% (17/209) • Control: 13.9% (29/208) RR 0.58, 95% CI: 0.33 to 1.03

First author, date	Efficacy outcomes	Safety outcomes
	RR 1.06, 95% CI: 0.87 to 1.30 ≥65 years • ECLS: 58.8% (50/85) • Control: 63.5% (61/96) RR 0.88, 95% CI: 0.61 to 1.28	**Stroke or systemic embolisation** • ECLS: 3.8% (8/209) • Control: 2.9% (6/208) RR 1.33, 95% CI: 0.47 to 3.76. **Repeat vascularisation** • ECLS: 8.6% (18/209) • Control: 10.6% (22/208) RR 0.81, 95% CI: 0.45 to 1.47
Banning, 2023	**30-day all-cause mortality** • ECMO: 43.8% (7/17) • Standard therapy: 61.1% (11/18) HR 0.56, 95% CI: 0.21 to 1.45; p=0.22 HR 0.40, 95% CI: 0.13 to 1.26; p=0.105 (as-treated analysis) **1 year all-cause mortality** • ECMO: 51.8% (8/17) • Standard therapy: 81.5% (14/18) HR 0.52, 95% CI: 0.21 to 1.26; p=0.14 **1 year readmission for heart failure** • ECMO: 8.0% (1/17) • Standard therapy: 6.9% (1/18) HR 1.19, 95% CI: 0.11 to 13.22; p=0.89) **HRQoL at 30 days EQ-5D-3L summary index** (median [IQR]) • ECMO: 0.667 (0.326 to 1.00)	**Complications (ITT analysis)** All-cause death: ECMO: 50% (7/14), Standard therapy: 72% (13/18) CV death: ECMO: 14% (2/14), Standard therapy: 33% (6/18) Stroke: ECMO: 0% (0/14), Standard therapy: 11% (2/18) Ischaemic stroke: ECMO: 0% (0/14), Standard therapy: 11% (2/18) Recurrent MI: ECMO: 0% (0/14), Standard therapy: 11% (2/18) Major bleeding: ECMO: 36% (5/14), Standard therapy: 6% (1/18) Escalation to non-VAECMO device for refractory shock ECMO: 0% (0/5), Standard therapy:17% (1/6) Escalation to VA ECMO: Standard therapy: 6% (1/18) Any vascular complications: ECMO: 21% (3/14), Standard therapy: 0 (0/18) Acute kidney injury: ECMO: 29% (4/14), Standard therapy:44% (8/18) Failure of discharge from primary admission: ECMO: 57% (8/14), Standard therapy:83% (15/18) **Serious adverse events** • ECMO: 9 events (6 patients [35.29%]) • Standard therapy: 13 events (5 patients [27.78%]) Cardiac events

First author, date	Efficacy outcomes	Safety outcomes
	• Standard therapy: 0.765 (0.739 to 0.790)	• ECMO: 5 (29.41%); cardiac arrest (1), cardiac tamponade (2), ventricular tachycardia (2), LV thrombus (1). • Standard therapy: 4 (22.2%); cardiac arrest (1), ventricular arrythmia (2), AV block (1), atrial fibrillation (1). <u>Respiratory and Thoracic events</u> • ECMO: 1 (5.88%); pulmonary embolism • Standard therapy: 2 (11.11%); aspiration pneumonia (1), thoracic haemorrhage (1) <u>Infection and infestation</u> • ECMO: 1 (5.88%); post procedural sepsis • Standard therapy: 2 (11.11%); Septic shock (1), Acinetobacter infection (1) <u>Gastrointestinal disorders</u> ECMO: 0 (0%), Standard therapy: 1 (5.56%); intestinal ischemia <u>Hepatobiliary disorders</u> ECMO: 0 (0%), Standard therapy: 1 (5.56%); liver injury <u>VA ECMO related syndromes</u> ECMO: 1 (5.88%); harlequin syndrome, Standard therapy: 0 (0%) <u>Surgical procedures</u> ECMO: 0 (0%), Standard therapy: 1 (5.56%); heart transplant <u>Vascular disorders</u> ECMO: 0 (0%), Standard therapy: 1 (5.56%); Peripheral ischemia
Ostadal, 2023	**Death from any cause, implantation of another MCS device, resuscitated cardiac arrest at 30 days** • ECMO: 63.8% (37/58) • Control: 71.2% (42/59) Risk difference -7.4, 95% CI: -24.3 to 9.5 HR 0.721, 95% CI: 0.463 to 1.123	**Resuscitated cardiac arrest** • ECMO: 10.3% (6/58) • Control: 13.6% (8/59) Risk difference -3.2, 95% CI: -15.0 to 8.5 HR 0.790, 95% CI: 0.274 to 2.277 **Serious adverse events** • ECMO: 60.3% (35/58)

First author, date	Efficacy outcomes	Safety outcomes
	All-cause mortality at 30 days • ECMO: 50.0% (29/58) • Control: 47.5% (28/59) Risk difference 2.5, 95% CI: -15.6 to 20.7 HR 1.110, 95% CI: 0.660 to 1.866 **Implantation of another MCS device at 30 days** • ECMO: 17.2% (10/58) • Control: 42.4% (25/59) Risk difference -25.1, 95% CI: -41.1 to -9.2 HR 0.380, 95% CI: 0.182 to 0.793 **Discharged home at 30 days** • ECMO: 12.1% (7/58) • Control: 11.9% (7/59) **Good neurological status at 30 days (CPC 1)** • ECMO: 24.1% (14/58) • Control: 27.1% (16/59)	• Control: 61.0% (36/59) Risk difference -0.7, 95% CI: -18.4 to 17.0; p=0.941 **Bleeding** • ECMO: 31.0% (18/58) • Control: 20.3% (12/59) Risk difference 10.7, 95% CI: -5.0 to 26.4; p=0.185 **Leg ischaemia** • ECMO: 13.8% (8/58) • Control: 5.1% (3/59) Risk difference 8.7, 95% CI: -1.8 to 19.2; p=0.107 **Stroke** • ECMO: 5.2% (3/58) • Control: 0% (0/59) Risk difference 5.2, 95% CI: -0.5 to 10.9; p=0.119 **Pneumonia** • ECMO: 31.0% (18/58) • Control: 30.5% (18/59) Risk difference 0.5, 95% CI: -16.2 to 17.3; p=0.951 **Sepsis** • ECMO: 39.7% (23/58) • Control: 39.0% (23/59) Risk difference 0.7, 95% CI: -17.0 to 18.4; p=0.941 **Technical complications** • ECMO: 1.7% (1/58) • Control: 0% (0/59) Risk difference 1.7, 95% CI: -1.6 to 5.1; p=0.496
Sohail, 2022	**Pooled short-term mortality (7 day, 30 day and in-hospital)** Meta-analysis 72 studies (n=10,276)	**ECMO Complications (median [IQR])** • Infection: 18.0% (11.8 to 43.0) • Limb ischaemia: 9.2% (7.6 to 15.0)

First author, date	Efficacy outcomes	Safety outcomes
	• 58% (95% CI: 54 to 61%), I^2=88% **Subgroup analysis short-term mortality by age** Meta-analysis 6 studies (n=497) • Age >60 years: OR 4.58 (95% CI: 2.71 to 7.72)	• Renal failure: 39.9% (29.5 to 49.8) • VTE: 4.7% (3.3 to 6.8) • Hypoxic brain injury: 11.6% (10.1 to 20.8) • Multi-organ failure: 36.9% (16.4 to 41.7) • Stroke/ICH: 10.5% (5.0 to 16.7) • Bleeding/vascular complications: 27.5% (19.0 to 35.4)
Alba, 2021	**Pooled short-term mortality (30 day and in-hospital)** • Overall: 61% (95% CI 59 to 63) 306 studies n=29,289 • ECPR OHCA: 76% (95% CI 69 to 82), I^2=94%, 41 studies n=2,974 • ECPR IHCA: 64% (95% CI 59 to 69), I^2=81%, 46 studies n=2,987 • Post AMI: 60% (95% CI 59 to 64), I^2=87%, 80 studies n=7,774 • Postcardiotomy: 59% (95% CI 56 to 63), I^2=87%, 64 studies n=8,231 • AHF: 53% (95% CI 46 to 59), I^2=89%, 33 studies n=3,567 • PE: 52% (95% CI 38 to 66), I^2=75%, 10 studies n=221 • Myocarditis: 40% (95% CI 33 to 46), I^2=65%, 13 studies n=906 • Post-HTx: 35% (95% CI 29 to 42), I^2=64%, 25 studies n=771 **Probability of HTx**	**No safety outcomes were reported**

First author, date	Efficacy outcomes	Safety outcomes
	Meta-analysis • AHF: 13.1%, 95% CI: 5.5 to 23.7, 16 studies • Myocarditis: 4.5%, 95% CI: 0.3 to 11.7, 5 studies • Post AMI: 2.8%, 95% CI: 0.8 to 5.5, 19 studies • Postcardiotomy: 0.4%, 95% CI: 0.0 to 1.1, 34 studies • Post-HTx: 0.0%, 95% CI: 0.0 to 0.5, 5 studies • PE: 0.0%, 95% CI: 0.0 to 22.8, 1 study **Probability of VAD** Meta-analysis • AHF: 29.0%, 95% CI: 17.3 to 42.1, 17 studies • Post AMI: 9.0%, 95% CI: 4.2 to 15.1, 22 studies • Post-HTx: 2.4%, 95% CI: 0.0 to 6.8, 5 studies • Myocarditis: 2.3%, 95% CI: 0.2 to 5.6, 5 studies • Postcardiotomy: 0.8%, 95% CI: 0.2 to 1.8, 35 studies • PE: 0.0%, 95% CI: 0.0−22.8, 1 study	
Cheng, 2019	**Survival to discharge** • 29.7% (149/502)	**Mortality after hospital discharge** • 14.1% (21/149)

First author, date	Efficacy outcomes	Safety outcomes
	Overall survival rate (Kaplan-Meier analysis probability at 3-years) after hospital discharge • All: 76.7% **Freedom-from-event rate including death or heart replacement therapy (Kaplan-Meier analysis probability at 3-years) after hospital discharge** • All: 74.2% • ADHF: 100% • Postcardiotomy CS: 85.5% • Allograft failure: 74.2% • AMI: 40.4% (p<0.001)	**Cause of death during follow-up period** • Sudden death or unknown cause: 9/21 • Heart failure related: 4/21 • Sepsis:4/21 • Chronic rejection: 3/21 • Stroke: 1/21
Vishram-Nielsen, 2023	**Pooled short-term mortality (30 days or during hospitalisation)** Meta-analysis 50 studies (n=2,470) • 34.68% (95% CI: 29.16 to 40.39), I^2=69% **Pooled short-term mortality (death on ECMO)** Meta-analysis 36 studies (n=945) • 27.03% (95% CI: 20.98 to 33.48), I^2=67% **Pooled VAD implantation after VA ECMO** Meta-analysis 22 studies (n=628) • 2.23% (95% CI: 0.13 to 5.85), I^2=67%	**Pooled neurological events** Meta-analysis 8 studies (n=375) • 7.40% (95% CI: 3.25 to 12.60), I^2=30% **Pooled infections** Meta-analysis 8 studies (n=323) • 34.83% (95% CI: 15.80 to 56.34), I^2=79% **Pooled limb ischaemia** Meta-analysis 6 studies (n=161) • 16.65% (95% CI: 5.78 to 30.65), I^2=69% **Pooled blood transfusions** Meta-analysis 2 studies (n=63) • 54.71% (95% CI: 0.00 to 100.00), I^2=96%

First author, date	Efficacy outcomes	Safety outcomes
	Pooled probability of HTx after VA ECMO Meta-analysis 23 studies (n=635) 3.71% (95% CI: 0.47 to 8.76), I^2=72%	**Pooled liver failure** Meta-analysis 2 studies (n=63) • 5.62% (95% CI: 0.41 to 14.20), I^2=0% **Pooled ventricular tachycardia or fibrillation** Meta-analysis 4 studies (n=270) • 22.57% (95% CI: 2.73 to 50.96), I^2=84% **Pooled 3rd degree atrioventricular block** Meta-analysis 3 studies (n=215) • 30.46% (95% CI: 0.00 to 78.46), I^2=93% **Pooled bleeding** Meta-analysis 6 studies (n=152) • 40.32% (95% CI: 22.89 to 58.92), I^2=76% **Pooled dialysis** Meta-analysis 6 studies (n=327) 35.22% (95% CI: 11.90 to 62.35), I^2=89%
Olson, 2020	**Survival to hospital discharge** • 63.6% (56/88) **ECMO weaning with expected recovery** • 61.4% (54/88) **ECMO weaning to HTx or VAD** • 10.2% (9/88)	**Cardiovascular complications** • 47.6% (30/63); cardiac arrythmia (12), hypertension requiring vasodilators (2), myocardial stun by echocardiogram (2), Inotropes on ECLS (26). **Haemorrhagic complications** • 49.2% (31/63); cannulation site bleeding (16), disseminated intravascular coagulation (2), GI haemorrhage (7), Haemolysis (4), surgical site bleeding (13). **Infectious complications** • 7.9% (5/63); culture proven infection (5), white blood cell count <1,500/µl (2) **Mechanical complications** • 33% (21/63); cannula problems (6), circuit clots (13), pump malfunction (1) **Metabolic complications**

First author, date	Efficacy outcomes	Safety outcomes
		• 11.1% (7/63); hyperglycaemia >240 mg/dl (2), hyperbilirubinemia (6), pH<7.20 (2) **Neurological complications** • 14.3% (9/63); seizures by EEG (2), CNS infarction (3), CNS haemorrhage (5) **Pulmonary complications** • 9.5% (6); Pneumothorax requiring treatment (3), pulmonary haemorrhage (3) **Renal complications** • 38.1% (24); renal replacement (16), creatinine elevation (12) **Limb complications** 7.9% (5); limb ischaemia (3), limb fasciotomy (2)

Procedure technique

Of the 10 studies, none detailed the ECMO device or combination of devices used. ECMO was started before percutaneous coronary intervention (PCI) in one randomised controlled trial of people with CS complicating AMI (Thiele 2023) but was started within 6 hours of randomisation in people who had already undergone PCI in another (Banning 2023). Left ventricular (LV) venting strategies were detailed in 6 studies (Thiele 2023, Banning 2023, Ostadal 2023, Sohail 2022, Alba 2021, Vishram-Neilsen 2023); 2 RCTs had a predefined criteria for LV venting and permitted insertion of an intra-aortic balloon pump (IABP) or Impella device (Thiele 2023, Banning 2023), another randomised controlled trial permitted LV unloading but strategies were left to the discretion of physicians at participating centres (Ostadal 2023). The median concomitant use of IABP reported in systematic reviews was 70% (Sohail 2022), 20 to 67% (Alba 2021) and 60% (Vishram-Neilsen 2023). Of the 10 studies, 6 detailed the median length of time on ECMO (Thiele 2023, Sohail 2022, Alba 2021, Cheng 2019, Vishram-Neilsen 2023, Olson 2020), which ranged from 2.7 days (Thiele 2023) to 10.5 days (Cheng 2019).

Efficacy

Survival

Survival was reported in 2 retrospective studies (Cheng 2019, Olson 2020). The retrospective study of 88 people with peripartum cardiomyopathy reported a rate of survival to hospital discharge of 64% (Olson 2020). In the randomised controlled trial of 117 people with CS complicating AMI, 12% of people in both the ECMO group and the control group had been discharged home at 30 days (Ostadal 2023).

In the single centre retrospective study, 30% (149 of 502) of people having VA ECMO survived to discharge (Cheng 2019). Of these survivors, the Kaplan-Meier estimate of survival at 3 years was 74% in the overall population but was statistically significantly lower ($p<0.001$) in people with AMI (40%) compared to those with ADHF (100%), postcardiotomy (86%), allograft failure (74%) (Cheng 2019).

Short-term mortality

Short-term mortality was reported in 7 studies, 4 of which included mortality at 30 days and 3 systematic reviews which pooled mortality results at 30 days and hospital discharge.

In the systematic review of 611 people with CS complicating AMI across 4 randomised controlled trials, the pooled 30-day mortality was 46% for those who had VA ECMO, compared to 48% in the control group. The relative risk (RR) was 0.95 (95% CI: 0.80 to 1.12; $p=0.54$, $I^2=0\%$) (Elsaeidy 2024).

In the randomised controlled trial of 417 people with CS complicating AMI, 47% of people who had ECMO and 49% of people in the control group reported death from any cause at 30 days. The RR was 0.98 (95% CI: 0.80 to 1.19; $p=0.81$; Thiele 2023). In the randomised controlled trial of 117 people with CS complicating AMI, all-cause mortality at 30 days was 50% in the ECMO group compared to 48% in the control group. The risk difference was 2.5 (95% CI -15.6 to 20.7) and HR 1.11 (95% CI 0.66 to 1.87) (Ostadal 2023). In the randomised controlled trial of 35 people with CS complicating AMI, 30-day all-cause mortality was 44% for those who had ECMO compared to 61% for those who had standard therapy. The hazard ratio (HR) was 0.56 (95% CI: 0.21 to 1.45; $p=0.22$). At 1 year follow-up, all-cause mortality was 52% in people who had ECMO, and 82% in those who had standard therapy (HR 0.52, 95% CI 0.21 to 1.26, $p=0.14$; Banning 2023). In the systematic review of 72 studies of CS complicating AMI,

the pooled short-term mortality (30-day and in-hospital) was 58% (95% CI: 54 to 61%), I^2=88% (Sohail 2022).

In a subgroup analysis by age in the randomised controlled trial of 417 people with CS complicating AMI, the 30-day all-cause mortality rate for those who had ECMO was 40% in those under 65 years, and 59% in those over 65 years (Thiele 2023). In a subgroup analysis by age in the systematic review of CS complicating AMI, age greater than 60 years was associated with increased mortality OR 4.58 (95% CI: 2.71 to 7.72; Sohail 2022).

In the systematic review of 306 studies of CS of any aetiology, the pooled overall short-term mortality (30-day and in-hospital) was 61% (95% CI 59 to 63) (Alba 2021). Pooled short-term mortality by CS aetiology subgroup, showed the highest mortality was in people with ECPR for out of hospital cardiac arrest (OHCA) (76%; 95% CI 69 to 82%, I^2=94%, 41 studies). This was followed by ECPR for in hospital CA (IHCA) at 64% (95% CI 59 to 69, I^2=81%, 46 studies), post-AMI at 60% (95% CI 59 to 64, I^2=87%, 80 studies), postcardiotomy at 59% (95% CI 56 to 63, I^2=87%, 64 studies). Pooled short-term mortality for people with acute decompensated heart failure (ADHF) was 53% (95% CI 46 to 59, I^2=89%, 33 studies), 52% in people with pulmonary embolism (95% CI 38 to 66, I^2=75%, 10 studies). It was lowest in people with myocarditis at 40% (95% CI 33 to 46), I^2=65%, 13 studies) and after heart transplant 35% (95% CI 29 to 42, I^2=64%, 25 studies). Using multivariate meta regression analysis, differences in short-term mortality across aetiologies remained statistically significant ($p<0.01$) after adjusting for population age, sex, and recruitment timeframe. Univariate meta regression analysis stratified by aetiology also showed a 7% to 9% increase in mortality per 10-year increase in cohort's age (Alba 2021).

In the systematic review of 54 studies in people with fulminant myocarditis, the pooled short-term mortality (30-day and in-hospital) was 35% (95% CI: 29 to 40,

I^2=69%, 50 studies). The pooled short-term mortality from 36 studies looking at death on ECMO was 27% (95% CI: 21 to 34, I^2=67%; Vishram-Nielsen 2023).

In the single centre retrospective study of 149 people who had survived VA ECMO explantation, 14% died after hospital discharge (median follow-up 306 days) (Cheng 2019).

Bridged to heart transplant

The proportion of people who had a heart transplant after ECMO treatment was reported in 3 systematic reviews and 1 registry study. In the systematic review of 306 studies in people on ECMO for CS of any aetiology, meta-analyses demonstrated the probability of having a heart transplant was higher in people with heart failure (13%), compared to those with myocarditis (5%), AMI (3%), and postcardiotomy CS (less than 1%; Alba 2021). In the systematic review of people with fulminant myocarditis, the pooled probability of heart transplant in a meta-analysis of 23 studies was 4% (95% CI: 0.47 to 8.76, I^2=72%; Vishal-Nielsen 2023). In the registry study of 88 people with peripartum cardiomyopathy, 10% were weaned from ECMO to either heart transplant or a VAD (Olson, 2020).

Bridged to long term device

The proportion of people receiving a ventricular assist device (VAD) after ECMO treatment was reported in 2 systematic reviews and 2 registry studies. In the systematic review of 306 studies in people on ECMO for CS, meta-analyses demonstrated the probability of receiving a VAD was higher in people with heart failure (29%), compared to those with AMI (9%), myocarditis (5%), heart transplant (2%) and postcardiotomy (1%; Alba 2021). In the systematic review of people with fulminant myocarditis, the pooled probability of heart transplant in a meta-analysis of 22 studies was 2% (95% CI: 0.47 to 8.76, I^2=72%; Vishal-Nielsen 2023). In the registry study of 88 people with peripartum cardiomyopathy, 10% were weaned from ECMO to either heart transplant or a VAD (Olson, 2020).

Reinfarction

In the systematic review of 4 randomised controlled trials for people with CS complicating AMI, pooled 30-day reinfarction rate was 2% in both the VA ECMO and control group (RR 0.87, 95% CI: 0.25 to 3.04; p=0.83, I^2=0%) (Elsaeidy 2024). In the randomised controlled trial of 417 people with CS complicating AMI, both intervention and control groups reported myocardial reinfarction rates of 1% (Thiele, 2023).

Rehospitalisation for heart failure

Two randomised controlled trials reported on the number of people who were readmitted to hospital because of heart failure. In the randomised controlled trial of 417 people with CS complicating AMI, 1% of people in both the ECMO group and control group were re-hospitalised within 30 days because of heart failure (Thiele, 2023). The randomised controlled trial of 35 people with CS complicating AMI reported a readmission rate for heart failure of 8% in the ECMO group and 7% in the standard therapy group at 1 year follow-up (Banning 2023).

Quality of life

One randomised controlled trial reported quality of life at 30 days using the EQ-5D-3L questionnaire, however few completed the questionnaire in both the standard therapy (n=2) and VA ECMO (n=4) groups. Among the respondents, the median summary index score for those on ECMO was 0.667 (0.326 to 1.00), and 0.765 (0.739 to 0.790) for those on standard therapy. In the standard therapy group, there were no reported problems with mobility, self-care, or usual activities at 30 days, while half of the respondents from the VA ECMO group reported some difficulties in these domains at 30 days (Banning, 2023).

Safety

Bleeding

In the systematic review of 4 randomised controlled trials, the pooled bleeding event rate was 25% (76 out of 302) in the ECMO group compared to 12% (36 out of 306) in the control group (RR 2.14, 95% CI: 1.49 to 3.07; p<0.0001, I^2=0%; Elsaeidy 2024). Moderate or severe bleeding was reported in 23% (49 out of 209) of people on ECMO compared to 12% (20 out of 208) of people in the control group (RR 2.44, 95% CI: 1.50 to 3.95) in the randomised controlled trial of 417 people with CS complicating AMI (Thiele 2023). Major bleeding was reported in 36% (5 out of 14) of people on ECMO and 6% (1 out of 18) of people in the control group in the randomised controlled trial of 35 people with CS complicating AMI (Banning 2023). Bleeding complications were reported in 31% (18 out of 58) of people on ECMO compared to 20% (12 out of 59) of the control group in the randomised controlled trial of 177 people with CS complicating AMI (Ostadal 2023). Pooled bleeding/vascular complication rates were 28% (19.0 to 35.4) in the systematic review of 72 studies with CS complicating AMI (Sohail, 2022).

A pooled bleeding event rate of 40% (95% CI: 22.89 to 58.92, I^2=76%) was reported in a meta-analysis of 6 studies in the systematic review of people with fulminant myocarditis on ECMO (Vishram-Nielsen 2023).

Bleeding complications were reported in 49% (31 out of 88) of people on ECMO with peripartum cardiomyopathy. Cannulation site bleeds were reported in 16 out of 88 people and surgical site bleeds in 13 out of 88 people (Olson 2020).

Renal replacement therapy or acute kidney injury

In the systematic review of 4 randomised controlled trials, the pooled acute kidney injury or RRT event rate was 9% (25 out of 281) in the ECMO group compared to 14% (40 out of 285) in the control group (RR 0.65, 95% CI: 0.41 to

1.04; p=0.07, I^2=0%; Elsaeidy 2024). RRT was reported in 8% (17 out of 209) of people on ECMO compared to 14% (29 out of 208) of people in the control group (RR 0.58, 95% CI: 0.33 to 1.03) in the randomised controlled trial of 417 people with CS complicating AMI (Thiele 2023). Acute kidney injury was reported in 29% (4 out of 14) of people on ECMO and 44% (8 out of 18) of people in the control group in the randomised controlled trial of 35 people with CS complicating AMI (Banning 2023). Pooled renal failure rates were 40% (16.4 to 41.7) in the systematic review of 72 studies with CS complicating AMI (Sohail, 2022).

A pooled RRT event rate of 35% (95% CI: 11.90 to 62.35, I^2=89%) was reported in a meta-analysis of 6 studies in the systematic review of people with fulminant myocarditis on ECMO (Vishram-Nielsen 2023).

Renal complications were reported in 38% (24 out of 88) people on ECMO with peripartum cardiomyopathy. RRT was reported in 16 out of 88 people (Olson 2020).

Stroke

In the systematic review of 4 randomised controlled trials, the pooled stroke event rate was 4% in both ECMO and control groups (12 out of 302 and 11 out of 306) (RR 1.14, 95% CI: 0.52 to 2.49; p=0.75, I^2=18%; Elsaeidy 2024). Stroke or systemic embolisation was reported in 4% (8 out of 209) of people on ECMO and 3% (6 out of 208) of people in the control group (RR 1.33, 95% CI: 0.47 to 3.76) in the RCT of 417 people with CS complicating AMI (Thiele 2023). Stroke was not reported in any people on ECMO (0 out of 14) but in 11% (2 out of 18) of people in the control group in the randomised controlled trial of 35 people with CS complicating AMI (Banning 2023). Conversely, in the randomised controlled trial of 177 people with CS complicating AMI, stroke was reported in 5% (3 out of 58) of people on ECMO and none in the control group in the (Ostadal 2023).

Pooled stroke rates were 11% (5.0 to 16.7) in the systematic review of 72 studies with CS complicating AMI (Sohail 2022).

A pooled neurological event rate of 7% (95% CI: 3.25 to 12.60, I^2=30%) was reported in a meta-analysis of 8 studies in the systematic review of people with fulminant myocarditis on ECMO (Vishram-Nielsen 2023).

Neurological complications were reported in 14% (9 out of 88) of people on ECMO with peripartum cardiomyopathy. CNS infarction was reported in 3 out of 88 people, and CNS haemorrhage in 5 out of 88 people (Olson 2020).

Of the 21 people who died after hospital discharge (median follow-up 306 days) in the single centre retrospective study of people who had initially survived VA ECMO explantation, 1 cause of death was reported as due to stroke (Cheng 2019).

Neurological outcome

One randomised controlled trial reported on the proportion of people with a good neurological outcome at 30 days, assessed as category 1 using the Cerebral Performance Category (CPC 1). In the study of 117 people with CS complicating AMI, the proportion of people assessed as CPC 1 was 24% in the ECMO group compared to 27% in the control group (Ostadal 2023).

One randomised controlled trial reported on the proportion of people with a poor neurological outcome at 30 days, assessed as category 3 or 4 using the Cerebral Performance Category (CPC 3 or 4). In the study of 417 people with CS complicating AMI, the proportion of people assessed as CPC 3 or 4 was 25% (27 out of 109) in the ECMO group compared to 23% (24 out of 106) in the control group (Thiele 2023).

Sepsis

In the systematic review of 4 randomised controlled trials, the pooled sepsis event rate was 18% (54 out of 305) in the ECMO group compared to 17% (51 out of 306) in the control group (RR 1.07, 95% CI: 0.77 to 1.48; p=0.85, I^2=0%; Elsaeidy 2024). Post-procedural sepsis was reported in 1 person on ECMO, and septic shock in 1 person in the control group in the randomised controlled trial of 35 people with CS complicating AMI (Banning 2023). Sepsis was reported in 40% (23 out of 58) of people on ECMO compared to 39% (23 out of 59) of the control group in the randomised controlled trial of 177 people with CS complicating AMI (risk difference 0.7, 95% CI: -17.0 to 18.4; p=0.941; Ostadal 2023).

Of the 21 people who died after hospital discharge (median follow-up 306 days) in the single centre retrospective study of people who had initially survived VA ECMO explantation, 4 causes of death were reported as due to sepsis (Cheng 2019).

Infection

The pooled median infection rate was 18% (11.8 to 43.0) in the systematic review of 72 studies with CS complicating AMI (Sohail 2022). A pooled infection event rate of 35% (95% CI: 15.80 to 56.34, I^2=79%) was reported in a meta-analysis of 8 studies in the systematic review of people with fulminant myocarditis on ECMO (Vishram-Nielsen 2023). Infectious complications were reported in 8% (5 out of 88) of people on ECMO with peripartum cardiomyopathy. Culture proven infection was reported in 5 out of 88 people, and white blood cell count <1,500/µl in 2 out of 88 people (Olson 2020).

Pneumonia

In the systematic review of 2 randomised controlled trials, the pooled pneumonia event rate was 24% (18 out of 75) in the ECMO group compared to 25% (19 out of 77) in the control group (RR 0.97, 95% CI: 0.57 to 1.65; p=0.90, I^2=0%;

Elsaeidy 2024). Pneumonia was reported in 31% (18 out of 58 and 18 out of 59) of people in both groups in the randomised controlled trial of 177 people with CS complicating AMI (risk difference 0.5, 95% CI: -16.2 to 17.3; p=0.951; Ostadal 2023).

Limb ischaemia

Peripheral ischaemic vascular complications were reported in 11% (23 out of 209) of people on ECMO compared to 4% (8 out of 208) of people in the control group (RR 2.86, 95% CI: 1.31 to 6.25) in the randomised controlled trial of 417 people with CS complicating AMI (Thiele 2023). Leg ischaemia was reported in 14% (8 out of 58) of people on ECMO compared to 5% (3 out of 59) of the control group in the randomised controlled trial of 177 people with CS complicating AMI (risk difference 8.7, 95% CI: -1.8 to 19.2; p=0.107; Ostadal 2023). Pooled limb ischaemia rates were 9% (7.6 to 15.0) in the systematic review of 72 studies with CS complicating AMI (Sohail 2022). The pooled limb ischaemia event rate of 17% (95% CI: 5.78 to 30.65, I^2=69%) was reported in a meta-analysis of 6 studies in the systematic review of people with fulminant myocarditis on ECMO (Vishram-Nielsen 2023). Limb complications were reported in 8% (5 out of 88) of people on ECMO with peripartum cardiomyopathy. Limb ischaemia was reported in 3 out of 88 people, and limb fasciotomy in 2 out of 88 people (Olson 2020).

Cardiac complications

Cardiovascular death was reported in 14% (2 out of 14) of people in the ECMO group, and 33% (6 out of 18) of people in the control group in the randomised controlled trial of 35 people with CS complicating AMI (Banning 2023). The same study reported recurrent MI in 11% (2 out of 18) people in the control group, and none in the ECMO group. It also reported 5 serious cardiac adverse events in people who had ECMO compared to 4 in those who had standard therapy. These included cardiac arrest, cardiac tamponade, ventricular tachycardia, LV

thrombus, AV block and atrial fibrillation (Banning 2023). Resuscitated cardiac arrest was reported in 10% (6 out of 58) of people in the ECMO group compared to 14% (8 out of 59) of the control group in the randomised controlled trial of 177 people with CS complicating AMI (risk difference -3.2, 95% CI: -15.0 to 8.5; Ostadal 2023).

A pooled ventricular tachycardia or fibrillation event rate of 23% (95% CI: 1.73 to 50.96; I^2=84%) was reported in a meta-analysis of 4 studies in the systematic review of people with fulminant myocarditis who had ECMO. The same systematic review also reported a pooled rate of third degree atrioventricular block of 23% (95% CI: 0.00 to 78.46; I^2=93%) from 3 studies (Vishram-Nielsen 2023).

Cardiovascular complications were reported in 48% (30 out of 88) of people on ECMO with peripartum cardiomyopathy. These included inotropes on ECMO, cardiac arrhythmia, hypertension requiring vasodilators and myocardial stun by echocardiogram (Olson 2020).

Of the 21 people who died after hospital discharge (median follow-up 306 days) in the single centre retrospective study of people who had initially survived VA ECMO explantation, 4 causes of death were reported as heart failure related (Cheng 2019).

Respiratory complications

The randomised controlled trial of 35 people with CS complicating AMI reported 1 serious respiratory adverse event in people on ECMO compared to 2 in those on standard therapy. These included pulmonary embolism, aspiration pneumonia and thoracic haemorrhage (Banning 2023).

Pulmonary complications were reported in 10% (9 out of 88) of people on ECMO with peripartum cardiomyopathy. This included pneumothorax requiring treatment and pulmonary haemorrhage (Olson 2020).

GI complications

The randomised controlled trial of 35 people with CS complicating AMI reported 1 serious gastrointestinal (GI) adverse event (intestinal ischaemia) in people on standard therapy (Banning 2023).

Hepatic complications

The randomised controlled trial of 35 people with CS complicating AMI reported 1 serious hepatobiliary adverse event (liver injury) in people on standard therapy (Banning 2023).

A pooled liver failure event rate of 6% (95% CI: 0.41 to 14.20; I^2=0%) was reported in a meta-analysis of 2 studies in the systematic review of people with fulminant myocarditis on ECMO (Vishram-Nielsen 2023).

Technical complications

Technical complications were reported in 2% (1 out of 58) of people on ECMO compared to none in the control group in the randomised controlled trial of 177 people with CS complicating AMI (risk difference 1.7, 95% CI: -1.6 to 5.1; p=0.496; Ostadal 2023).

Mechanical complications were reported in 33% (21 out of 88) of people on ECMO with peripartum cardiomyopathy. These included cannula problems, circuit clots, and pump malfunctions (Olson 2020).

Anecdotal and theoretical adverse events

Expert advice was sought from consultants who have been nominated or ratified by their professional society or royal college. They were asked if they knew of

any other adverse events for this procedure that they had heard about (anecdotal), which were not reported in the literature. They were also asked if they thought there were other adverse events that might possibly occur, even if they had never happened (theoretical).

They listed the following anecdotal and theoretical adverse events:

- Left ventricle overloading
- Deep vein thrombosis
- Arteriovenous fistula
- Pseudoaneurysm
- Harlequin syndrome
- Haemolysis
- Intracerebral haemorrhage
- Major pulmonary bleed
- Failure to cannulate during cardiac arrest
- Malposition of the cannula
- Device clotting
- Air entrainment/embolus
- Embolism
- Oxygenator failure
- Consumption coagulopathy
- Acquired Von Willebrand syndrome
- Systemic inflammatory response syndrome (SIRS)
- Multi-organ failure including kidney, liver, and pancreas.

Sixteen professional expert questionnaires were submitted. Find full details of what the professional experts said about the procedure in the specialist advice questionnaires for this procedure.

Validity and generalisability

- Most of the studies included in the key evidence had a large number of participants from a variety of countries.
- Due to the impact of the COVID-19 pandemic, the Banning (2023) trial was stopped before completion of recruitment, and therefore had a small sample size (n=35). Olson (2020) study also included a relatively small population (n=88); however, this was the largest study sample identified for the postpartum cardiomyopathy indication.
- Follow-up for most studies were short, reporting key efficacy outcomes at 30 days, or at hospital discharge. One retrospective study reporting on ECMO as a bridge to recovery had a longer follow-up period (Cheng 2019).
- The systematic reviews included as key evidence pooled short-term mortality outcomes (30 day, hospital discharge) from included studies.
- CS can have many aetiologies with different risk profiles and outcomes. Most studies included in this review focus on CS complicating AMI, however other included studies report populations with mixed CS aetiologies.
  - People having ECMO for decompensated AHF, myocarditis, peri-partum cardiomyopathy may have better outcomes than people with AMI complicating CS.
- The randomised controlled trials included recruited participants with different classifications of CS; Thiele (2023) included those with SCAI classification C, which is considered much lower risk, than SCAI D and E, which were included in the Ostadal (2023) study.
- A large proportion of people in the control groups in the included randomised controlled trials were permitted other MCS such as IABP and Impella. In the

Ostadal (2023) trial there was also a large amount of cross-over of the control group to receive ECMO (39%).

Ongoing trials

- Assessment of ECMO in Acute Myocardial Infarction Cardiogenic Shock (ANCHOR) (NCT04184635); open label randomised controlled trial, France, n=400, completion October 2026.
- Left Ventricular Unloading to Improve Outcome in Cardiogenic Shock Patients on VA ECMO (UNLOAD ECMO) (NCT05577195), randomised controlled trial, Germany, n=198, completion December 2025.

Related NICE guidance

Interventional procedures

Extracorporeal membrane oxygenation (ECMO) for acute heart failure in adults (2014) NICE interventional procedures guidance [IPG 482]. (Recommendation: special arrangements).

NICE guidelines

Acute heart failure: diagnosis and management (2014 updated 2021) NICE guideline CG187 - At an early stage, the specialist should have a discussion with a centre providing mechanical circulatory support about: people with potentially reversible severe acute heart failure or people who are potential candidates for transplantation.

Professional societies

- The Intensive Care Society
- Society for Cardiothoracic Surgery in Great Britain & Ireland
- Royal College of Anaesthetists

- Royal College of Surgeons
- Faculty of Intensive Care Medicine
- British Society for Heart Failure
- NHS Blood and Transplant
- British cardiovascular society
- European Extracorporeal Life Support Organisation

Company engagement

NICE asked companies who manufacture a device potentially relevant to this procedure for information on it. NICE received 2 completed submissions. These were considered by the interventional procedures technical team and any relevant points have been taken into consideration when preparing this overview.

References

1. Elsaeidy, Ahmed Saad, Taha, Amira Mohamed, Abuelazm, Mohamed et al. (2024) Efficacy and safety of extracorporeal membrane oxygenation for cardiogenic shock complicating myocardial infarction: a systematic review and meta-analysis. BMC cardiovascular disorders 24(1): 362
2. Thiele, Holger, Zeymer, Uwe, Akin, Ibrahim et al. (2023) Extracorporeal Life Support in Infarct-Related Cardiogenic Shock. The New England journal of medicine 389(14): 1286-1297
3. Banning, Amerjeet S, Sabate, Manel, Orban, Martin et al. (2023) Venoarterial extracorporeal membrane oxygenation or standard care in patients with cardiogenic shock complicating acute myocardial infarction: the multicentre, randomised EURO SHOCK trial. EuroIntervention: journal of EuroPCR in collaboration with the Working Group on Interventional Cardiology of the European Society of Cardiology 19(6): 482-492
4. Ostadal, P, Rokyta, R, Karasek, J et al. (2023) Extracorporeal Membrane Oxygenation in the Therapy of Cardiogenic Shock: results of the ECMO-CS Randomized Clinical Trial. Circulation 147(6): 454-464
5. Sohail, Shahmir, Fan, Eddy, Foroutan, Farid et al. (2022) Predictors of Mortality in Patients Treated with Veno-Arterial ECMO for Cardiogenic Shock Complicating Acute Myocardial Infarction: a Systematic Review and

Meta-Analysis. Journal of cardiovascular translational research 15(2): 227-238

6. Alba, Ana C, Foroutan, Farid, Buchan, Tayler A et al. (2021) Mortality in patients with cardiogenic shock supported with VA ECMO: A systematic review and meta-analysis evaluating the impact of etiology on 29,289 patients. The Journal of heart and lung transplantation: the official publication of the International Society for Heart Transplantation 40(4): 260-268
7. Cheng, Yi-Tso, Garan, Arthur R, Sanchez, Joseph et al. (2019) Midterm Outcomes of Bridge-to-Recovery Patients After Short-Term Mechanical Circulatory Support. The Annals of thoracic surgery 108(2): 524-530
8. Vishram-Nielsen, Julie K K, Foroutan, Farid, Rizwan, Saima et al. (2023) Patients with fulminant myocarditis supported with veno-arterial extracorporeal membrane oxygenation: a systematic review and meta-analysis of short-term mortality and impact of risk factors. Heart failure reviews 28(2): 347-357
9. Olson, T L, O'Neil, E R, Ramanathan, K et al. (2020) Extracorporeal membrane oxygenation in peripartum cardiomyopathy: A review of the ELSO Registry. International journal of cardiology 311: 71-76

Appendix A: Methods and literature search strategy

Methods and literature search strategy

NICE has identified studies and reviews relevant to extracorporeal membrane oxygenation (ECMO) for acute heart failure in adults from the medical literature.

Search strategy design and peer review

This search report is informed by the Preferred Reporting Items for Systematic reviews and Meta-Analyses literature search extension (PRISMA-S).

A NICE information specialist ran the literature searches on 18th September 2024. See the search strategy history for the full search strategy for each database. Relevant published studies identified during consultation or resolution that are published after this date may also be considered for inclusion.

The principal search strategy was developed in MEDLINE ALL (Ovid interface). It was adapted for use in each of the databases listed in table 4a, taking into account the database's size, search functionality and subject coverage. The MEDLINE ALL strategy was quality assured by a NICE senior information specialist. All translated search strategies were peer reviewed to ensure their accuracy. The quality assurance and peer review procedures were adapted from the Peer Review of Electronic Search Strategies (PRESS) 2015 evidence-based checklist.

Review management

The search results were managed in EPPI-Reviewer version 5 (EPPI-R5). Duplicates were removed in EPPI-R5 using a 2-step process. First, automated deduplication was done using a high-value algorithm. Second, manual deduplication was used to assess low-probability matches. All decisions about inclusion, exclusion and deduplication were recorded and stored.

Limits and restrictions

The CENTRAL database search removed trial registry records and conference material. The Embase search excluded conference material. We excluded the following publication types in MEDLINE: letter or historical article or comment or editorial or news or case reports. We excluded letters and editorial from the Embase search. English language limits were applied to the search when possible in the database.

The search was limited from March 2013 to September 2024. The date limit was included to update searches undertaken for an earlier version of this guidance.

The limit to remove animal studies in the searches is standard NICE practice, which has been adapted from Dickersin K, Scherer R, Lefebvre C (1994) Systematic Reviews: Identifying relevant studies for systematic reviews. BMJ 309(6964): 1286.

Main search

Table 4a Main search results

Database	Date searched	Database platform	Database segment or version	Number of results downloaded
Cochrane Central Register of Controlled Trials (CENTRAL)	18/08/24	Wiley	Issue 8 of 12, August 2024	410
Cochrane Database of Systematic Reviews (CDSR)	20/08/24	Wiley	Issue 9 of 12, September 2024	13
Embase	20/08/24	Ovid	1974 to 2024 September 17	2101
INAHTA International HTA Database	18/09/24	https://database.inahta.org/	-	24
MEDLINE ALL	18/09/24	Ovid	1946 to Sept 17, 2024	1454

[MEDLINE ALL] search strategy

1 , Heart Failure/th , 29,868

2 , Acute disease/th , 1,194

3 , 1 and 2 , 11

4 , *Cardiomyopathies/th , 1,150

5 , *Shock cardiogenic/th , 2,135

6 , Myocardial Stunning/th [Therapy] , 155

7 , Myocarditis/th [Therapy] , 1,294

8 , *Myocardial infarction/ , 138,977

9 , Out-of-Hospital Cardiac Arrest/th [Therapy] , 5,734

10 , ((acute* or server*) adj (heart* or cardiac* or myocard* or cardio* or ventric*) adj (failur* or decompensation* or insufficient* or dysfunct* or stand* or still* or fault* or shock*)).ti,ab. , 9,513

11 , Myocardit*.ti,ab. , 21,440

12 , ((Postpartum* or post-parttum* or peripartum* or peri-partum*) adj cardiomyopath*).ti,ab. , 1,697

13 , PPCM.ti,ab. , 671

14 , (myocard* adj (stun* or hibernat* or infract*)).ti,ab. , 2,258

15 , Primary Graft Dysfunction/th [Therapy] , 99

16 , (primary* adj graft* adj dysfunct*).ti,ab. , 1,392

17 , or/3-16 , 182,062

18 , *Cardiopulmonary Resuscitation/mt [Methods] , 4,116

19 , *Extracorporeal Membrane Oxygenation/ , 13,895

20 , ECMO.ti. , 3,217

21 , *Extracorporeal Circulation/mt [Methods] , 1,090

22 , (extracorp* adj circulat*).ti,ab. , 8,596

23 , (extracorp* adj ((cardiopulmon* adj resuscitat*) or CPR)).ti,ab. , 1,229

24 , ECPR.ti. , 154

25 , (Biomedicus adj pump*).ti,ab. , 45

26 , (Maquet* adj rotaflow*).ti,ab. , 12

27 , (jostra adj (pump* or rotaflow*)).ti,ab. , 5

28 , (levitronix adj (centrimag* or pump* or system* or oxygen*)).ti,ab. , 54

29 , (Medos adj (Hilite* or oxygen*)).ti,ab. , 22

30 , left ventricle assist device.ti,ab. , 106

31 , or/18-30 , 28,477

32 , 17 and 31 , 2,725

33 , animals/ not human/ , 5,225,551

34 , 32 not 33 , 2,680

35 , limit 34 to english language , 2,503

36 , limit 35 to ed=20130331-20240930 , 2,028

37 , limit 36 to (letter or historical article or comment or editorial or news or case reports) , 574

38 , 36 not 37 , 1,454

[Embase] search strategy

1 , heart failure/th [Therapy] , 15,752

2 , acute disease/th [Therapy] , 2,395

3 , 1 and 2 , 10

4 , *cardiomyopathy/th [Therapy] , 1,144

5 , *cardiogenic shock/th [Therapy] , 2,129

6 , stunned heart muscle/th [Therapy] , 53

7 , myocarditis/th [Therapy] , 864

8 , *heart infarction/ , 110,365

9 , primary graft dysfunction/th [Therapy] , 94

10 , "out of hospital cardiac arrest"/th [Therapy] , 3,862

11 , ((acute* or server*) adj (heart* or cardiac* or myocard* or cardio* or ventric*) adj (failur* or decompensation* or insufficient* or dysfunct* or stand* or still* or fault* or shock*)).ti,ab. , 17,537

12 , Myocardit*.ti,ab. , 31,093

13 , ((Postpartum* or post-parttum* or peripartum* or peri-partum*) adj cardiomyopath*).ti,ab. , 2,835

14 , PPCM.tw. , 1,261

15 , (myocard* adj (stun* or hibernat* or infract*)).ti,ab. , 3,555

16 , (primary* adj graft* adj dysfunct*).tw. , 3,009

17 , or/3-16 , 173,201

18 , *resuscitation/ , 60,473

19 , *extracorporeal oxygenation/ , 16,545

20 , ECMO.ti. , 7,837

21 , *extracorporeal circulation/ , 9,094

22 , (extracorp* adj circulat*).ti,ab. , 9,683

23 , (extracorp* adj ((cardiopulmon* adj resuscitat*) or CPR)).ti,ab. , 1,851

24 , ECPR.ti. , 352

25 , (Biomedicus adj pump*).ti,ab. , 50

26 , (Maquet* adj rotaflow*).ti,ab. , 31

27 , (jostra adj (pump* or rotaflow*)).ti,ab. , 16

28 , (levitronix adj (centrimag* or pump* or system* or oxygen*)).ti,ab. , 150

29 , (Medos adj (Hilite* or oxygen*)).ti,ab. , 44

30 , left ventricle assist device.ti,ab. , 217

31 , or/18-30 , 96,434

32 , 17 and 31 , 5,350

33 , Nonhuman/ not Human/ , 5,532,522

34 , 32 not 33 , 5,275

35 , limit 34 to letter/ or (letter or editorial).pt. , 2,165,352

36 , 34 not 35 , 4,904

37 , limit 36 to dc=20130331-20240930 , 3,599

38 , limit 37 to english language , 3,481

39 , (conference abstract* or conference review or conference paper or conference proceeding).db,pt,su. , 6,020,541

40 , 38 not 39 , 2,101

Cochrane Library (CDSR) search strategy

#1 MeSH descriptor: [Heart Failure] explode all trees and with qualifier(s): [therapy - TH] 2591

#2 MeSH descriptor: [Acute Disease] explode all trees and with qualifier(s): [therapy - TH] 118

#3 #1 and #2 0

#4 MeSH descriptor: [Cardiomyopathies] explode all trees and with qualifier(s): [therapy - TH] 248

#5 MeSH descriptor: [Shock, Cardiogenic] explode all trees and with qualifier(s): [therapy - TH] 177

#6 MeSH descriptor: [Myocardial Stunning] explode all trees and with qualifier(s): [therapy - TH] 3

#7 MeSH descriptor: [Myocarditis] explode all trees and with qualifier(s): [therapy - TH] 13

#8 MeSH descriptor: [Myocardial Infarction] explode all trees and with qualifier(s): [therapy - TH] 3337

#9 MeSH descriptor: [Primary Graft Dysfunction] explode all trees and with qualifier(s): [therapy - TH] 3

#10 MeSH descriptor: [Out-of-Hospital Cardiac Arrest] explode all trees and with qualifier(s): [therapy - TH] 539

#11 ((acute* or server*) near/1 (heart* or cardiac* or myocard* or cardio* or ventric*) near/1 (failur* or decompensation* or insufficient* or dysfunct* or stand* or still* or fault* or shock*)) 2663

#12 Myocardit* 1421

#13 (Postpartum* or post-partum* or peripartum* or peri-partum*) near/1 cardiomyopath* 47

#14 PPCM 39

#15 (myocard* near/1 (stun* or hibernat* or infract*)) 342

#16 (primary* near/1 graft* near dysfunct*) 146

#17 #3 or #4 or #5 or #6 or #7 or #8 or #9 or #10 or #11 or #12 or #13 or #14 or #15 or #168646

#18 MeSH descriptor: [Cardiopulmonary Resuscitation] this term only 1688

#19 MeSH descriptor: [Extracorporeal Membrane Oxygenation] this term only 361

#20 ECMO 1101

#21 MeSH descriptor: [Extracorporeal Circulation] this term only and with qualifier(s): [methods - MT]120

#22 (extracorp* near/1 circulat*) 1423

#23 (extracorp* near/1 ((cardiopulmon* near resuscitat*) or CPR)) 71

#24 ECPR 112

#25 (Biomedicus near/1 pump*) 3

#26 (Maquet* rotaflow*) 3

#27 jostra near/1 (pump* or rotaflow*) 1

#28 (levitronix near/1 (centrimag* or pump* or system* or oxygen*)) 0

#29 Medos near/1 (Hilite* or oxygen*) 0

#30 left ventricle assist device 219

#31 #18 or #19 or #20 or #21 or #22 or #23 or #24 or #25 or #26 or #27 or #28 or #29 or #304577

#32 #17 AND #31 494

#33 "conference":pt or (clinicaltrials or trialsearch):so 777352

#34 #32 NOT #33 with Cochrane Library publication date Between Mar 2013 and Sep 2024, in Cochrane Reviews 13

[Cochrane Library CENTRAL)] search strategy

#1 MeSH descriptor: [Heart Failure] explode all trees and with qualifier(s): [therapy - TH] 2591

#2 MeSH descriptor: [Acute Disease] explode all trees and with qualifier(s): [therapy - TH] 118

#3 #1 and #2 0

#4 MeSH descriptor: [Cardiomyopathies] explode all trees and with qualifier(s): [therapy - TH] 248

#5 MeSH descriptor: [Shock, Cardiogenic] explode all trees and with qualifier(s): [therapy - TH] 177

#6 MeSH descriptor: [Myocardial Stunning] explode all trees and with qualifier(s): [therapy - TH] 3

#7 MeSH descriptor: [Myocarditis] explode all trees and with qualifier(s): [therapy - TH] 13

#8 MeSH descriptor: [Myocardial Infarction] explode all trees and with qualifier(s): [therapy - TH] 3337

#9 MeSH descriptor: [Primary Graft Dysfunction] explode all trees and with qualifier(s): [therapy - TH] 3

#10 MeSH descriptor: [Out-of-Hospital Cardiac Arrest] explode all trees and with qualifier(s): [therapy - TH] 539

#11 ((acute* or server*) near/1 (heart* or cardiac* or myocard* or cardio* or ventric*) near/1 (failur* or decompensation* or insufficient* or dysfunct* or stand* or still* or fault* or shock*)) 2663

#12 Myocardit* 1421

#13 (Postpartum* or post-partum* or peripartum* or peri-partum*) near/1 cardiomyopath* 47

#14 PPCM 39

#15 (myocard* near/1 (stun* or hibernat* or infract*)) 342

#16 (primary* near/1 graft* near dysfunct*) 146

#17 #3 or #4 or #5 or #6 or #7 or #8 or #9 or #10 or #11 or #12 or #13 or #14 or #15 or #168646

#18 MeSH descriptor: [Cardiopulmonary Resuscitation] this term only 1688

#19 MeSH descriptor: [Extracorporeal Membrane Oxygenation] this term only 361

#20 ECMO 1101

#21 MeSH descriptor: [Extracorporeal Circulation] this term only and with qualifier(s): [methods - MT] 120

#22 (extracorp* near/1 circulat*) 1423

#23 (extracorp* near/1 ((cardiopulmon* near resuscitat*) or CPR)) 71

#24 ECPR 112

#25 (Biomedicus near/1 pump*) 3

#26 (Maquet* rotaflow*) 3

#27 jostra near/1 (pump* or rotaflow*) 1

#28 (levitronix near/1 (centrimag* or pump* or system* or oxygen*)) 0

#29 Medos near/1 (Hilite* or oxygen*) 0

#30 left ventricle assist device 219

#31 #18 or #19 or #20 or #21 or #22 or #23 or #24 or #25 or #26 or #27 or #28 or #29 or #304577

#32 #17 AND #31 494

#33 "conference":pt or (clinicaltrials or trialsearch):so 777352

#34 #32 NOT #33 with Cochrane Library publication date Between Mar 2013 and Sep 2024, in Trials 410

[INAHTA HTA Database] search strategy

1 , "Heart Failure"[mh] , 252

2 , "Acute Disease"[mh] , 46

3 , #2 AND #1 , 2

4 , "Cardiomyopathies"[mh] , 21

5 , "Shock, Cardiogenic"[mh] , 11

6 , "Myocardial Stunning"[mh] , 1

7 , "Myocarditis"[mh] , 1

8 , "Myocardial Infarction"[mh] , 123

9 , "Out-of-Hospital Cardiac Arrest"[mh] , 10

10 , ((acute* or server*) and (heart* or cardiac* or myocard* or cardio* or ventric*) and (failur* or decompensation* or insufficient* or dysfunct* or stand* or still* or fault* or shock*)). , 149

11 , Myocardit* , 5

12 , ((Postpartum* or post-parttum* or peripartum* or peri-partum*) AND cardiomyopath*) , 1

13 , PPCM , 0

14 , (myocard* and (stun* or hibernat* or infract*)) , 2

15 , "Primary Graft Dysfunction"[mh] , 0

16 , (primary* AND graft* AND dysfunct*). , 3

17 , #16 OR #15 OR #14 OR #13 OR #12 OR #11 OR #10 OR #9 OR #8 OR #7 OR #6 OR #5 OR #4 OR #3 , 291

18 , "Cardiopulmonary Resuscitation"[mh] , 23

19 , "Extracorporeal Membrane Oxygenation"[mh] , 29

20 , ECMO , 31

21 , "Extracorporeal Circulation"[mh] , 9

22 , (extracorp* AND circulat*). , 13

23 , (extracorp* AND ((cardiopulmon* AND resuscitat*) or CPR)) , 8

24 , ECPR , 4

25 , (Biomedicus AND pump*). , 0

26 , Maquet* and rotaflow*) , 0

27 , (jostra and (pump* or rotaflow*)). , 0

28 , (levitronix AND (centrimag* or pump* or system* or oxygen*)). , 0

29 , (Medos AND (Hilite* or oxygen*)). , 0

30 , left ventricle assist device , 3

31 , #30 OR #29 OR #28 OR #27 OR #26 OR #25 OR #24 OR #23 OR #22 OR #21 OR #20 OR #19 OR #18 , 74

32 , #31 AND #17 , 24

Inclusion criteria

The following inclusion criteria were applied to the abstracts identified by the literature search.

- Publication type: clinical studies were included with emphasis on identifying good quality studies. Abstracts were excluded if they did not report clinical outcomes. Reviews, editorials, and laboratory or animal studies, were also excluded and so were conference abstracts, because of the difficulty of appraising study methodology, unless they reported specific adverse events not available in the published literature.
- People with acute heart failure.
- Intervention or test: VA ECMO.
- Outcome: articles were retrieved if the abstract contained information relevant to the safety, efficacy, or both.

If selection criteria could not be determined from the abstracts the full paper was retrieved.

Potentially relevant studies not included in the main evidence summary are listed in Appendix B: Other relevant studies.

Find out more about how NICE selects the evidence for the committee.

Appendix B: Other relevant studies

Other potentially relevant studies that were not included in the main evidence summary (tables 2 and 3) are listed in table 5 below.

Case studies and observational studies with fewer than 100 people were excluded unless they included outcomes that were not frequently reported.

Table 5 additional studies identified

Study	Number of people and follow up	Direction of conclusions	Reason study was not included in main evidence summary
Briglio SE, Khanduja V, Lothan JD et al. (2024) Fulminant myocarditis and venoarterial extracorporeal membrane oxygenation: a systematic review. Cureus *16*(2): e54711	Systematic review n=425 11 studies	Regarding short-term outcomes, one-year post-hospital survival rate ranged from 57.1% to 78% at discharge. For long-term health and survival, studies that recorded long-term survival ranged from 65% to 94.1%.	No meta-analysis.
Burgos LM, Seoane L, Diez M et al. (2023) Multiparameters associated to successful weaning from VA ECMO in adult patients with cardiogenic shock or cardiac arrest: Systematic review and meta-analysis. Annals of cardiac anaesthesia 26(1): 4-11	Systematic review and meta-analysis n=653 11 studies Follow-up: weaning, hospital discharge	Pooled VA ECMO successful weaning [patient survives 48 hours after ECMO explantation] was 45% (95% CI: 39 to 50%, I^2 7%) and in-hospital mortality rate was 46.6% (95% CI: 33 to 60%; I^2 36%).	Larger, more comprehensive systematic literature reviews and meta-analysis included. 5/11 studies in this SLR were included within the SLRs in the key evidence.
Carroll BJ, Shah RV, Murthy V et al. (2015) Clinical features and	Single centre retrospective study, US	Overall, 69 people (56%) were weaned from ECMO, with 48	More recent studies included.

outcomes in adults with cardiogenic shock supported by extracorporeal membrane oxygenation. The American journal of cardiology 116(10): 1624-30	n=123 (26 postcardiotomy [21%]) Follow-up: In-hospital	patients (39%) surviving to discharge.	
Cheng R, Hachamovitch R, Kittleson M et al. (2014) Clinical outcomes in fulminant myocarditis requiring extracorporeal membrane oxygenation: a weighted meta-analysis of 170 patients. Journal of cardiac failure 20(6): 400-6	Systematic review and meta-analysis n=170 6 studies	The pooled estimate rate of survival to hospital discharge was 66.9% (95% CI 59.4% to 73.7%). More than two-thirds of patients with FM and either cardiogenic shock and/or cardiac arrest survive to hospital discharge with ECMO.	More recent systematic reviews and meta-analyses included. 4/6 studies in this SLR were included within the SLRs in the key evidence.
Cheng R, Hachamovitch R, Kittleson M et al. (2014) Complications of extracorporeal membrane oxygenation for treatment of cardiogenic shock and cardiac arrest: A meta-analysis of 1,866 adult patients. Annals of Thoracic Surgery 97(2): 610-616	Systematic review and meta-analysis n=1,866 20 studies Follow-up: Hospital discharge	Seventeen studies reported survival to hospital discharge, range: 20.8% to 65.4%.	More recent systematic reviews and meta-analyses included. 7/20 studies in this SLR were included within the SLRs in the key evidence.
Danial P, Olivier M-E, Brechot N et al. (2023) Association between shock etiology and 5-year outcomes after venoarterial extracorporeal membrane oxygenation. Journal of the American College of Cardiology 81(9): 897-909	Single centre retrospective study, US n=1,253 Follow-up: in-hospital, 5 years	In-hospital and 5-year survival rates were, respectively, 73.3% and 57.3% for primary graft failure, 58.6% and 54.0% for drug overdose, 53.2% and 45.3% for dilated cardiomyopathy, 51.6% and 50.0% for arrhythmic storm, 46.8% and 38.3% for massive pulmonary embolism, 44.4% and	Larger, more comprehensive systematic literature reviews and meta-analysis included.

		42.4% for sepsis-induced cardiogenic shock, 37.9% and 32.9% for fulminant myocarditis, 37.3% and 31.5% for acute myocardial infarction, 34.6% and 33.3% for postcardiotomy excluding primary graft failure, 25.7% and 22.8% for other/unknown aetiology, and 11.1% and 0.0% for refractory vasoplegia shock.	
Dangers L, Brechot N, Schmidt M et al. (2017) Extracorporeal membrane oxygenation for acute decompensated heart failure. Critical Care Medicine 45(8): 1359-1366	Single centre retrospective study, France n=105 Follow-up: 1 year	Survival at 1 year was 42%, with 44% of the cohort receiving heart transplantation. Survival was considerably lower (17%) in people with a high pre-ECMO SOFA score (≥14), than those with SOFA score less than 7 (52%).	More recent studies from broader regions included.
Flecher E, Anselmi A, Corbineau H et al. (2014) Current aspects of extracorporeal membrane oxygenation in a tertiary referral centre: determinants of survival at follow-up. European Journal of Cardio-thoracic Surgery: official journal of the European Association for Cardio-thoracic Surgery 46(4): 665-671	Single centre retrospective study, France n=325 (postcardiotomy 29%) Follow-up: mean 84 days (SD: 86)	Overall in the VA group, weaning rates were 59%, survival at 30th post implantation day was 44% and survival at the end of the follow-up was 41%.	More recent studies with outcomes split by aetiologies were included.
Hernandez-Montfort JA, Xie R, Ton VK et al. (2020) Longitudinal impact of temporary mechanical circulatory	Retrospective INTERMACS registry study. n=13,813 Follow-up:	INTERMACS Profile 1 to 3 patients with pre-implant ECMO had 82% survival at 1 month and 44% at 48	Registry studies with more relevant outcomes were included.

support on durable ventricular assist device outcomes: An IMACS registry propensity matched analysis. The Journal of Heart and Lung Transplantation: the official publication of the International Society for Heart Transplantation 39(2): 145-156	48 months	months. 22% people requiring ECMO needed biventricular support after dVAD.	
Lackermair K, Brunner S, Orban M et al. (2021) Outcome of patients treated with extracorporeal life support in cardiogenic shock complicating acute myocardial infarction: 1-year result from the ECLS-Shock study. Clinical Research in Cardiology: official journal of the German Cardiac Society 110(9): 1412-1420	Randomised controlled trial n=42 Follow-up: 12 months	12-month all-cause mortality was numerically lower, and favourable neurological outcome numerically higher in the ECLS arm compared to the no ECLS arm.	Pilot study, superseded by Thiele, 2023 ECLS-SHOCK study
Lee JH, Choi N, Kim YJ et al. (2021) Use of extracorporeal life support for heart transplantation: Key factors to improve outcome. Journal of Clinical Medicine 10(12): 2542	Single centre retrospective study, Korea. n=257 (100 ECLS) Follow-up: 30 days and 12 months after HTx	The 30-day mortality rate was 3.9% (9.2% in peripheral ECLS, 2.9% in central ECLS, and 1.9% in non-ECLS). The use of ECLS was not an independent predictor of 30-day and 1-year mortality (p = 0.248 and p = 0.882, respectively).	Larger, more comprehensive systematic literature reviews and meta-analysis included.
Lorusso R, Gelsomino S, Parise O et al. (2017) Venoarterial extracorporeal membrane oxygenation for refractory cardiogenic shock in elderly patients: trends	Retrospective ELSO registry study. n=5,408 (735 ≥70 years) Follow-up: hospital	Survival to hospital discharge for the entire adult cohort was 41.4%, with 30.5% (224/735) in the elderly patient group and 43.1% (2,016 of 4,673) in the younger patient	Larger, more comprehensive registry studies were included.

in application and outcome from the Extracorporeal Life Support Organization (ELSO) Registry. Annals of Thoracic Surgery 104(1): 62-69	discharge	group (p<0.001). Elderly patients had a higher rate of multiorgan failure. At multivariable analysis age represented an independent negative predictor of in-hospital survival.	
Loungani RS, Fudim M, Ranney D et al. (2021) Contemporary use of venoarterial extracorporeal membrane oxygenation: insights from the multicenter RESCUE registry. Journal of cardiac failure 27(3): 327-337	Retrospective RESCUE registry study. n=723 Follow-up: hospital discharge	40% of the cohort survived to discharge, Mortality for ECMO following heart transplant (42.4%) and cardiomyopathy (59.3%) was less than those receiving ECMO for postcardiotomy CS (64%), AMI (60.7%).	Larger, more comprehensive registry studies were included.
Loyaga-Rendon RY, Boeve T, Tallaj J et al. (2020). Extracorporeal membrane oxygenation as a bridge to durable mechanical circulatory support: an analysis of the STS-INTERMACS Database. Circulation. Heart failure, 13(3), e006387.	Retrospective INTERMACS registry study. n=19,824 Follow-up: 2 years	In adult patients who received a durable MCS who were supported with and without VA ECMO, ECMO patients had inferior survival at 12 months (66%) than non-ECMO patients (75%; p<0.0001).	Registry studies with more relevant outcomes were included.
Mastoris I, Tonna JE, Hu J et al. (2022) Use of extracorporeal membrane oxygenation as bridge to replacement therapies in cardiogenic shock: insights from the Extracorporeal Life Support Organization. Circulation. Heart failure 15(1): e008777	Retrospective ELSO registry study n=401 Follow-up: unclear	All-cause hospital mortality was 28.9% for people who received ECMO prior to Heart transplant or LVAD. In those receiving LVAD mortality was 28.7% and heart transplant mortality was 29.1%.	Larger, more comprehensive registry studies were included.
Morrow DA and van Diepen S (2022) The extracorporeal	Randomised controlled trial	There was no significant difference between the two arms	Summary of ECMO-CS trial reported fully

membrane oxygenation in the therapy of cardiogenic shock (ECMO-CS) trial in perspective. European Heart Journal. Acute cardiovascular care 11(12): 933-935	n=117 Follow-up: 30 days	for all-cause death at 30 days.	in Ostadal, 2023
Movahed MR, Soltani MA, Hashemzadeh M (2024) In patients with cardiogenic shock, extracorporeal membrane oxygenation is associated with very high all-cause inpatient mortality rate. Journal of Clinical Medicine 13(12): 3607	Retrospective study of US National Inpatient Sample database. n=13,160	Total inpatient mortality 47.9% with ECMO. In a multivariate analysis adjusting for 47, ECMO utilisation remained highly associated with mortality (OR: 1.78, 95% CI: 1.6 to 1.9, p<0.001). Higher complications associated with the use of ECMO including bleeding, thromboembolic events, infections, and neurologic and vascular complications may contribute to higher mortality.	More comprehensive registry studies, which included CS aetiologies were included.
North M, Samara M, Eckman PM et al. (2022) Survivors of veno-arterial membrane oxygenation have good long-term quality of life. The International journal of artificial organs 45(10): 826-832	Single centre retrospective study, US n=178 surveys (87% VA ECMO) Follow-up: 9 months	Minnesota Living with Heart Failure Questionnaire (MLWHFQ) total scores improved over time (51.7 at 3 months, vs 37.7 at 6 months, vs 25.4 at greater than 9 months; p<0.01)	Larger registry studies with more relevant outcomes are included.
Nunez JI, Grandin EW, Reyes-Castro T et al. (2023) Outcomes with peripheral venoarterial extracorporeal membrane oxygenation for suspected acute myocarditis: 10-year experience from the Extracorporeal Life	Retrospective ELSO registry study n=850 Follow-up: Hospital discharge	During the study period, in-hospital mortality was 58.3% for all all-comers receiving VA ECMO compared with 34.9% for patients with myocarditis (*P*<0.001). 1.8% and 2.4% of patients were bridged	More comprehensive registry studies, which included more CS aetiologies were included.

Support Organization Registry. Circulation: Heart Failure 16(7): e010152		to heart transplant or LVAD respectively.	
Orbo MC, Karlsen SF, Pedersen EP et al. (2019) Health-related quality of life after extracorporeal membrane oxygenation: a single centre's experience. ESC heart failure 6(4): 701-710	Single centre retrospective study (Norway) n=74 (87% VA ECMO) Follow-up: Mean 6.5 years since ECMO	41% survival rate identified. 75% reported mental HRQoL (SF-36 Mental Component Summary, mean= 43, SD=5) or physical HRQL (SF-36 Physical Component Summary, mean=43, SD=4.5) within the normal range in comparison with age-matched population data from national norms. All but one responder lived independently without any organized care, and 90% reported no problems related to basic self-care. Half of those in working age had returned to work after ECMO treatment. Responders reported some degree of restrictions in usual daily activities (40%), problems with mobility (35%), anxiety/ depression (35%), or pain/ discomfort (55%). Improved HRQoL was significantly related to an extended time since ECMO treatment.	Larger registry studies with more relevant outcomes are included.
Ouweneel DM, Schotborgh JV, Limpens J et al. (2016) Extracorporeal life support during cardiac arrest and cardiogenic	Systematic review and meta-analysis n=3,333 (CA=3,098, CS after	In cardiac arrest, the use of ECLS was associated with an increased survival rate as well as an increase in favourable	More recent systematic reviews and meta-analyses included.

shock: a systematic review and meta-analysis. Intensive care medicine 42(12): 1922-1934	AMI=235),13 studies Follow-up: 30 days	neurological outcome. In the setting of cardiogenic shock there was an increased survival with ECLS compared with IABP.	
Paddock S, Meng J, Johnson N, Chattopadhyay R et al. (2024) The impact of extracorporeal membrane oxygenation on mortality in patients with cardiogenic shock post-acute myocardial infarction: a systematic review and meta-analysis. European Heart Journal Open; 4(1)	Systematic review and meta-analysis n=1,622 11 studies Follow-up: 30 days, 12 months	Meta-analysis demonstrates no significant difference in 30-day all-cause mortality with VA-ECMO compared with standard medical therapy (OR 0.91; 95% CI 0.65 to 1.27). Qualitative synthesis of the observational studies showed that age, serum creatinine, serum lactate, and successful revascularization are independent predictors of mortality.	Meta-analysis includes same RCTs as Elsaeidy et al. study included in key evidence but does not include safety data.
Sahli SD, Kaserer A, Braun J et al. (2022) Predictors associated with mortality of extracorporeal life support therapy for acute heart failure: single-center experience with 679 patients. Journal of Thoracic Disease 14(6): 1960-1971	Single centre retrospective study, Switzerland n=679 (postcardiotomy n=215) Follow-up: In-hospital	In-hospital mortality significantly varied between ECLS indications: 70.7% (152/215) for postcardiotomy, 67.9% (108/159) for cardiopulmonary resuscitation, 47.0% (110/234) for refractory cardiogenic shock, and 9.9% (7/71) for lung transplantation and expansive thoracic surgery (P<0.001).	Larger studies split by CS aetiology were included.
Schmidt M, Burrell A, Roberts L et al. (2015) Predicting survival after ECMO for refractory cardiogenic shock: the survival after veno-arterial-ECMO (SAVE)-	Retrospective ELSO registry study n=3,846 Follow-up: Hospital	1,601 (42%) patients were alive at hospital discharge. Chronic renal failure, longer duration of ventilation prior to ECMO initiation, pre-ECMO	More recent registry studies were included.

score. European heart journal, *36*(33), 2246–2256	discharge	organ failures, pre-ECMO cardiac arrest, congenital heart disease, lower pulse pressure, and lower serum bicarbonate were risk factors associated with mortality.	
Truby L, Mundy L, Kalesan B et al. (2015) Contemporary outcomes of venoarterial extracorporeal membrane oxygenation for refractory cardiogenic shock at a large tertiary care center. ASAIO journal (American Society for Artificial Internal Organs: 1992) 61(4): 403-9	Single centre retrospective study, US. n=179 (100 ECLS) Follow-up: 30 days and hospital discharge	Overall, 38.6% of patients survived to discharge and 44.7% of patients survived to 30 days. Myocardial recovery was achieved in 79.7% of survivors and 39.1% were transitioned to a more durable device.	Larger more recent registry studies were included.
Wang AS, Nemeth S, Vinogradsky A et al. (2022) Disparities in the treatment of cardiogenic shock: does sex matter?. European journal of cardio-thoracic surgery: official journal of the European Association for Cardio-thoracic Surgery 62(6)	Retrospective ELSO registry study n=9,888 (68% male) Follow-up: Hospital discharge	After propensity score matching, there was no difference in in-hospital mortality. Female patients were more likely to experience limb ischaemia, whereas males were more likely to receive renal replacement therapy and have longer hospital stays. Multivariable logistic regression confirmed sex was not independently associated with mortality.	Registry studies with more relevant outcomes are included.
Weiner L, Mazzeffi MA, Hines EQ et al. (2020) Clinical utility of venoarterial-	Retrospective ELSO registry study n=104	52.9% of the cases survived to discharge. VA ECMO significantly improved	Larger, more comprehensive registry studies were included.

extracorporeal membrane oxygenation (VA ECMO) in patients with drug-induced cardiogenic shock: a retrospective study of the Extracorporeal Life Support Organizations' ECMO case registry. Clinical toxicology (Philadelphia, Pa.) 58(7): 705-710	Follow-up: Hospital discharge	haemodynamics, acidaemia/ acidosis and ventilatory parameters. Non-survivors showed persistent acidaemia/ acidosis at 24 hours after VA ECMO cannulation compared to survivors. Renal replacement therapy (50.9%) and arrhythmia (26.3%) were the most frequently reported complications.	
Wilson-Smith AR, Bogdanova Y, Roydhouse S et al. (2019) Outcomes of venoarterial extracorporeal membrane oxygenation for refractory cardiogenic shock: systematic review and meta-analysis. Annals of cardiothoracic surgery, 8(1), 1–8.	Systematic review and meta-analysis n=17,515, 52 studies Follow-up: 5 years	Aggregated survival rates at 1, 2, 3, 4 and 5 years were 36.7%, 34.8%, 33.8%, 31.7% and 29.9%, respectively.	Larger, more recent SLRs for multi-aetiology CS included with more comprehensive outcomes.
Zaki HA, Yigit Y, Elgassim M et al. (2024) A systematic review and meta-analysis unveiling the pivotal role of extracorporeal membrane oxygenation (ECMO) in drug overdose treatment optimization. Bulletin of emergency and trauma, 12(3), 103–110.	Systematic review and meta-analysis n=694,10 studies Follow-up: Hospital discharge	The pooled analysis of ECMO in drug-overdosed/ poisoned people showed survival to hospital discharge rate of 65.6% (95% CI: 51.5% to 77.4%, p=0.030). However, the outcomes were highly heterogeneous (I^2=83.47%), which could be attributed to the use of several medicines by different studies. ECMO was associated with a rate of adverse events of 23.1% (95% CI: 12.3%	Larger, more comprehensive systematic literature reviews and meta-analysis included.

		to 39.2%, p=0.002).	
Zavalichi MA, Nistor I, Nedelcu A-E et al. (2020) Extracorporeal membrane oxygenation in cardiogenic shock due to acute myocardial infarction: a systematic review. BioMed Research International 2020: 6126534	Systematic review and meta-analysis n=1,998, 9 studies Follow-up: hospital discharge, 12 months	Survival rate varied from 30.0% to 79.2% at discharge and from 23.2% to 36.1% at 12 months. Reported serious adverse events were gastrointestinal bleeding (3.6%) and peripheral complications (8.5%).	No meta-analysis included.
Zhigalov K, Sa MPBO, Safonov D et al. (2020) Clinical outcomes of venoarterial extracorporeal life support in 462 patients: Single-center experience. Artificial organs 44(6): 620-627	Single centre retrospective study, Germany n=462 (postcardiotomy n=357) Follow-up: In-hospital	Overall, the in-hospital survival rate was 26%. There was no statistically significant difference between the groups: 26.3% for PCS and 24.8% for non-PCS, respectively (p>0.05). Weaning from VA-ECLS was possible in 44.3% for PCS and in 29.5% for non-PCS (p=0.004).	Larger studies split by CS aetiology were included.