NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

INTERVENTIONAL PROCEDURES PROGRAMME

Interventional procedure overview of extracorporeal membrane oxygenation (ECMO) for acute heart failure in adults

Heart failure can be caused by a number of factors that make the heart a less efficient pump. Extracorporeal membrane oxygenation (ECMO) is similar to a heart–lung bypass machine (used during heart surgery), which both pumps and oxygenates blood. Unlike a heart–lung bypass machine it tends to be used for days and not hours, allowing time for the heart to recover.

Introduction

The National Institute for Health and Care Excellence (NICE) has prepared this overview to help members of the Interventional Procedures Advisory Committee (IPAC) make recommendations about the safety and efficacy of an interventional procedure. It is based on a rapid review of the medical literature and specialist opinion. It should not be regarded as a definitive assessment of the procedure.

Date prepared

This overview was prepared in March 2013.

Procedure name

- Extracorporeal membrane oxygenation (ECMO) for acute heart failure in adults.

Specialist societies

- Intensive Care Society
- Society for Cardiothoracic Surgeons in Great Britain and Ireland
- Faculty of Intensive Care Medicine
- British Society for Heart Failure
- NHS Blood and Transplant.

Description

Indications and current treatment

Heart failure is a complex clinical syndrome of symptoms and signs that occurs when the efficiency of the heart as a pump is impaired. It can lead to reduced blood flow to the body tissues and increased filling pressure in the heart, which causes congestion and oedema in the lungs (causing breathlessness) and/or the body (causing swelling of the legs). Other symptoms include reduced exercise tolerance, fatigue and malaise.

The most common cause of heart failure in the UK is coronary artery disease. Around 900,000 people in the UK have heart failure. It has a poor prognosis: 30–40% of patients diagnosed with heart failure die within a year – but thereafter the mortality is less than 10% per year. There is evidence of a trend towards improved prognosis, with the 6-month mortality rate decreasing from 26% in 1995 to 14% in 2005.

Treatment for acute heart failure (specifically, sudden significant deterioration in people with known cardiac dysfunction or new onset of symptoms in people without previous cardiac dysfunction) involves pharmacological therapies, including diuretics and inotropic agents. Invasive therapies include electrophysiological intervention such as pacemakers or implantable cardioverter-defibrillators, revascularisation procedures such as percutaneous coronary intervention, valve replacement or repair, and temporary use of intra-aortic balloon pumps or ventricular assist devices.

What the procedure involves

ECMO for acute heart failure in adults can be used after heart surgery to assist in the transition from cardiopulmonary bypass to ventilation. It may also be used as a bridge to myocardial recovery, cardiac transplantation or implantation of a left ventricular assist device.

There are two main types of ECMO: venovenous ECMO (for respiratory support) and venoarterial ECMO (for cardiac and mixed cardiac and respiratory support). In venoarterial ECMO, blood is withdrawn via the venous system (usually the femoral vein or right atrium) and pumped through an oxygenator, where gas exchange of oxygen and carbon dioxide takes place. It is then returned to the arterial system (usually the femoral artery or ascending aorta). In both systems patients are given a continuous infusion of an anticoagulant, usually heparin, to prevent blood clotting in the external system. For patients with renal insufficiency, a hemofiltration unit may be integrated into the circuit.

Outcome measures

The New York Heart Association (NYHA) functional classification system categories are based on the patient’s quality of life and ability to perform everyday activities:

- classes I and II describe mild heart failure with no or slight limitation of physical activity
- class III describes moderate heart failure with marked limitation of physical activity
- class IV describes severe heart failure, when patients are unable to carry out any physical activity without discomfort.

Literature review

Rapid review of literature

The medical literature was searched to identify studies and reviews relevant to ECMO for acute heart failure in adults. Searches were conducted of the following databases, covering the period from their commencement to 26 March 2013: MEDLINE, PREMEDLINE, EMBASE, Cochrane Library and other databases. Trial registries and the Internet were also searched. No language restriction was applied to the searches (see appendix C for details of search strategy). Relevant published studies identified during consultation or resolution that are published after this date may also be considered for inclusion.

The following selection criteria (table 1) were applied to the abstracts identified by the literature search. Where selection criteria could not be determined from the abstracts the full paper was retrieved.

Table 1 Inclusion criteria for identification of relevant studies

Characteristic	Criteria
Publication type	Clinical studies were included. Emphasis was placed on identifying good quality studies. Abstracts were excluded where no clinical outcomes were reported, or where the paper was a review, editorial, or a laboratory or animal study. Conference abstracts were also excluded because of the difficulty of appraising study methodology, unless they reported specific adverse events that were not available in the published literature.
Patient	Adults with acute heart failure.
Intervention/test	Extracorporeal membrane oxygenation (ECMO).
Outcome	Articles were retrieved if the abstract contained information relevant to the safety and/or efficacy.
Language	Non-English-language articles were excluded unless they were thought to add substantively to the English-language evidence base.

List of studies included in the overview

This overview is based on 4038 patients from 10 case series[1-10] and 1 case report[11].

Other studies that were considered to be relevant to the procedure but were not included in the main extraction table (table 2) have been listed in appendix A.

Table 2 Summary of key efficacy and safety findings on extracorporeal membrane oxygenation (ECMO) for acute heart failure in adults

Abbreviations used: AM, acute myocarditis; ARDS, acute respiratory distress syndrome; AVR, aortic valve replacement; CABG, coronary artery bypass graft; CBP, cardiopulmonary bypass; CPR, cardiopulmonary resuscitation; DIC, disseminated intravascular coagulation; DCM, dilated cardiomyopathy; HF, heart failure; ICU, intensive care unit; HRQoL, health related quality of life; IABP, intra-aortic balloon pump; IQR, interquartile range; IV, intravenous; MOF, multiple organ failure; NYHA, New York Heart Association functional classification; OR, odds ratio; PCCS, postcardiotomy cardiogenic shock; SOFA, Sequential Organ Failure Assessment score; VAD, ventricular assist device.

<table>
<tr><th>Study details</th><th>Key efficacy findings</th><th>Key safety findings</th><th>Comments</th></tr>
<tr>
<td>Doll N (2004)[1]
Case series
Germany
Recruitment period: 1997-02
Study population: patients with refractory PCCS.
n = 219
Age: 61 years
Sex: 73% male

Patient selection criteria: ECMO candidates if cardiac index <2.0l/min, use of multiple inotropic agents and insertion of an IABP.

Technique: ECMO (pump: Vortex CN80, BioMedicus, Medtronic; oxygenator: Affinity, Omnis AOT) performed through the femoral vessels or</td>
<td>Number of patients analysed: 219
Survival (to discharge): 24%(52/219)
Independent predictors of in-hospital survival included younger age, use of IABP and absence of preoperative myocardial infarction.

Survival (at 5 year follow-up): 16.8% (37/219); (74% [37/50] of those who were discharged).
Independent predictors of survival at 5 years were younger age and absence of diabetes mellitus.
<table>
<tr><th>Outcomes</th><th>Days
mean (SD)</th></tr>
<tr><td>Duration of ECMO</td><td>2.8 (2.2)</td></tr>
<tr><td>Mechanical ventilation</td><td>11.5 (13.8)</td></tr>
<tr><td>ICU stay</td><td>15.0 (18.8)</td></tr>
<tr><td>Post-ECMO hospital stay</td><td>29.9 (24)</td></tr>
<tr><td></td><td>%(n)</td></tr>
<tr><td>Successful weaning</td><td>61 (133); 39% of these patients (52/133) subsequently discharged after a mean of 30 days.</td></tr>
<tr><td>Weaning unsuccessful</td><td>39 (86); ECMO support withdrawn and patients subsequently died.</td></tr>
<tr><td>Bridge to long-term VAD</td><td>4 (8); 5 died,2 successfully transplanted, and
1 successfully weaned</td></tr>
<tr><td>Mortality (5 years)</td><td>82(numbers not reported)</td></tr>
</table>
</td>
<td>
<table>
<tr><th>Complications</th><th>%(n/219)</th></tr>
<tr><td>Death (30-days)[a]</td><td>76(167)</td></tr>
<tr><td>Mediastinal bleeding (needing rethoracotomy)</td><td>62(136)</td></tr>
<tr><td>Renal failure</td><td>58(127);
56% (122) needed haemofiltration; no further details on the remaining patients</td></tr>
<tr><td>Infection (no further details provided)</td><td>24(52)</td></tr>
<tr><td>Lower limb ischaemia</td><td>13(28); fasciotomy for severe leg ischaemia was needed in 6%(13) of the patients.</td></tr>
<tr><td>Change of oxygenator (oxygenators were monitored for clots and changed if perfusion pressure increased)</td><td>22(48)</td></tr>
<tr><td>Neurological complications:</td><td></td></tr>
<tr><td>Cerebral oedema</td><td>5.9(13)</td></tr>
<tr><td>Cerebral haemorrhage</td><td>5.0(11)</td></tr>
<tr><td>Cerebral Infarction</td><td>4.6(10)</td></tr>
</table>
[a]causes: low cardiac output syndrome secondary to refractory myocardial failure (71%; n=118); MOF (14%;n=24), cerebral infarction/bleeding (5%;n=8), sepsis (4%;n=6), ARDS(2.5%; n=4), DIC (1%; n=2), bowel ischaemia (1%;n=2), pulmonary embolism (1%;n=2) and penetration of the endotracheal tube into the oesophagus (0.5%;n=1)
</td>
<td>Follow-up issues:
• Follow up available for 96% (50/52) of patients discharged.
Study design issues:
• Prospective study
• Survival calculated by Kaplan-Meier method.

Study population issues:
• Patients underwent CABG alone (54%), CABG plus AVR (10%),AVR (11%),CABG plus mitral valve replacement (5%) and other procedures, including pulmonary embolectomy, aortic aneurysm repair, heart transplant, ventricular septal defect closure (20%).
Other issues:
• Outcomes reported separately for the 5 surgical groups. There was no significant difference between groups in relation to duration of ECMO support, ability to wean</td>
</tr>
</table>

Abbreviations used: AM, acute myocarditis; ARDS, acute respiratory distress syndrome; AVR, aortic valve replacement; CABG, coronary artery bypass graft; CBP, cardiopulmonary bypass; CPR, cardiopulmonary resuscitation; DIC, disseminated intravascular coagulation; DCM, dilated cardiomyopathy; HF, heart failure; ICU, intensive care unit; HRQoL, health related quality of life; IABP, intra-aortic balloon pump; IQR, interquartile range; IV, intravenous; MOF, multiple organ failure; NYHA, New York Heart Association functional classification; OR, odds ratio; PCCS, postcardiotomy cardiogenic shock; SOFA, Sequential Organ Failure Assessment score; VAD, ventricular assist device.

Study details	Key efficacy findings	Key safety findings	Comments
through the right atrium and ascending aorta. ECMO instituted in operating room (89%) or ICU (11%). IABP was applied in 66% of patients. Follow-up: **5 years** Conflict of interest/source of funding: not reported.	**NYHA functional class** (at 5 years) Baseline: 3.4 (SD 0.8) Follow up(n=37) : class II **Repeat admission:** 14 patients (6 for cardiac investigations, 6 for non-cardiac-related surgical interventions and 2 for pneumonia).		from ECMO and ventilation time. • There was no significant difference between the groups in terms of incidence of sepsis, neurologic complications, bleeding needing mediastinal exploration and red blood cell transfusion. • Patients receiving ECMO support for combined CABG and AVR had a significantly higher mortality rate**.**

Abbreviations used: AM, acute myocarditis; ARDS, acute respiratory distress syndrome; AVR, aortic valve replacement; CABG, coronary artery bypass graft; CBP, cardiopulmonary bypass; CPR, cardiopulmonary resuscitation; DIC, disseminated intravascular coagulation; DCM, dilated cardiomyopathy; HF, heart failure; ICU, intensive care unit; HRQoL, health related quality of life; IABP, intra-aortic balloon pump; IQR, interquartile range; IV, intravenous; MOF, multiple organ failure; NYHA, New York Heart Association functional classification; OR, odds ratio; PCCS, postcardiotomy cardiogenic shock; SOFA, Sequential Organ Failure Assessment score; VAD, ventricular assist device.

Study details

Hoefer D (2006)[2]
Case series
Austria
Recruitment period: 1995-2005
Study population: patients with cardiogenic shock
n = **131**
Age: mean 49 years (range 14-70)
Sex: 67% male

Patient selection criteria: ECMO for intractable cardiogenic shock.

Technique: ECMO performed through femoral vessels with continuous heparin infusion. In case of weaning failure, patients considered for VAD after 72 hours.

Follow-up: **mean 39 months**

Conflict of interest/source of funding: not reported.

Key efficacy findings

Number of patients analysed: **131**

Outcomes: all ECMO patients (n=131)

Outcomes	%(n)	ECMO duration days; median (IQR)
Successful weaning[a]	35(46)	2.5(1-5)
Bridge to bridge (VAD implantation)[b]	21 (28) (mean assist time: 50 days)	3 (2-10)
Heart transplant (during ECMO support)	4 (5)	3 (2-7)
Overall survival (at mean 39 months)	50 (14) of the bridge to bridge patients	

[a]postcardiotomy HF 53.2%; acute HF 22.4%
[b]3 patients were weaned from VAD (bridge to recovery) and 11 patients underwent heart transplant (bridge to transplant).

Outcomes: bridge to bridge patients (n=28; outcomes reported for 14 patients; remaining died)

Outcomes	%(n)	ECMO duration days; median (IQR)
Weaning (bridge to recovery)	11 (3)	3 (2-5)
Heart transplant (bridge to transplantation)	39 (11) (total assist time: 77 days)	2 (1-3)

NYHA class (in survivors)
Baseline NYHA class not reported. After ECMO:NYHA class 1: 12 (no impairments in daily life) ; NYHA class II: 2.

Key safety findings

Death during ECMO support (n=131):
40% (52/131) (in 'most' cases because of MOF or sepsis)

Death during VAD support (n=28):
50% (14/28) (cause: MOF with sepsis [n=12]; intracranial bleeding [n=1]; bleeding during VAD explantation and attempted heart transplantation [n=1])

Complications after ECMO implantation	n
Bleeding needing surgical revision	8
Intrathoracal bleeding needing surgical revision	5
Clot formation (needing changes to oxygenator)	5
Femoral artery perforation (leading to uncontrollable bleeding and subsequent death)	2
Leg ischaemia because of thrombosis needing surgical revision	2
Aortic dissection (subsequent stent implantation)	2
Atrial thrombus	1

Comments

Study design issues:
- Retrospective review

Study population issues:
- Aetiologies: postcardiotomy HF: 48%(inability to wean from CBP after cardiac surgery or postoperative acute HF);acute HF 44%(including acute coronary ischaemia, myocarditis and near drowning); and acute on chronic HF :8%(known ischaemic or DCM).

Other issues:
- Outcomes reported for survivors and non survivors showed significant difference for variables including status post-CPR, cardiac output before ECMO. Aetiology of HF did not show significant influence on survival.

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Study details

Thiagarajan RR (2009)[3]
Case series (data from Extracorporeal Life Support Organization registry)
USA
Recruitment period: 1992-2007
Study population: ECMO used to support CPR in patients >18 years.
Diagnostic groups: acute myocardial infarction (36%), cardiomyopathy (19%), AM (5%), acute pulmonary embolism (4%), other cardiac disease (10%), miscellaneous (10%), respiratory (8%), accidental injury (5%), and sepsis (1%).
n = **295**
Age: median 52 years
Sex: 66% male
Patient selection criteria: Patients >18 years for whom ECMO was

Key efficacy findings

Number of patients analysed: **295**

Median duration of ECMO: 67 hours (IQR 21-133)

Survival to discharge (either to home or another facility) :27%(79/295)

Multivariate model- factors associated with mortality

	OR (95% CI)
Pre-ECMO factors	
Diagnostic groups	
Non cardiac diagnosis	1.00
Acute myocardial infarction	0.91(0.37 to 2.22)
Cardiomyopathy	0.88(0.31 to 2.48)
AM[a]	0.18(0.05 to 0.69)
Acute pulmonary embolism	0.32(0.08 to 1.32)
Other cardiac diseases	1.88(0.44 to 7.98)
Partial pressure of oxygen in arterial blood (mm Hg)	
≥149	1.00
70 to <149	2.34 (0.96 to 5.74)
<70[b]	2.70(1.21 to 6.07)
Percutaneous cannulation technique[b]	0.42(0.21 to 0.87)
ECMO complications:	
Need for dialysis[c]	2.41 (1.34 to 4.34)
ECMO duration (hours)	1.0 (1.0 to 1.00)

[a]p=0.01; [b]p=0.02;[c] p=0.003

Key safety findings

Complications	**Survivors (n=79); %(n)**	**Nonsurvivors (n=216);%(n)**
ECMO circuit:		
Mechanical problems	28(22)	34(73)
Clots in the ECMO circuit	17(13)	20(43)
Air embolus	1(1)	2(4)
Cannula site bleeding	19(15)	21(46)
Surgical bleeding	22(17)	25(54)
Central Nervous System:		
Brain death[a]	0	28(61)
Infarction or haemorrhage (radiologic evidence)	8(6)	13(27)
Seizures	3(2)	5(10)
Cardiac:		
CPR on ECMO	9(7)	13(27)
Arrhythmias on ECMO	27(21)	21(46)
Cardiac tamponade	6(5)	11(24)
Pulmonary:		
Pneumothorax	0	4(9)
Haemorrhage	1(1)	6(12)
Infection (culture proven)	18(14)	22(47)
Renal:		
need for dialysis[b]	24(19)	43(93)
Gastrointestinal:		
haemorrhage	4(3)	4(9)

[a]p<0.001; [b]p=0.003.

Comments

Study design issues:
- Retrospective
- Data on neurologic outcomes and technique, duration or medication used during CPR were not reported in the register.

Study population issues:
- The register defined ECMO supported CPR as where ECMO was used as part of initial resuscitation from cardiac arrest. Patients who were haemodynamically unstable and placed on ECMO without cardiac arrest were not considered.
- There were no significant differences between survivors and non survivors in relation to age, gender but survival varied significantly by diagnostic categories (improved survival in patients with AM) and by year of ECMO use (higher

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Study details	Key efficacy findings	Key safety findings	Comments
used to support for all CPR. Technique: veno arterial (91%) ECMO with femoral artery (81%) and femoral vein (70%) as the most common access sites for cannulation (33% percutaneous technique). Follow-up: **unclear** Conflict of interest/source of funding: not reported			proportion of non survivors in 2004-07)

Abbreviations used: AM, acute myocarditis; ARDS, acute respiratory distress syndrome; AVR, aortic valve replacement; CABG, coronary artery bypass graft; CBP, cardiopulmonary bypass; CPR, cardiopulmonary resuscitation; DIC, disseminated intravascular coagulation; DCM, dilated cardiomyopathy; HF, heart failure; ICU, intensive care unit; HRQoL, health related quality of life; IABP, intra-aortic balloon pump; IQR, interquartile range; IV, intravenous; MOF, multiple organ failure; NYHA, New York Heart Association functional classification; OR, odds ratio; PCCS, postcardiotomy cardiogenic shock; SOFA, Sequential Organ Failure Assessment score; VAD, ventricular assist device.

<table>
<tr><th>Study details</th><th>Key efficacy findings</th><th>Key safety findings</th><th>Comments</th></tr>
<tr>
<td>Paden ML (2013)[4]
Extracorporeal Life Support Organization register
1990-2012
(All patients entered before July 2012 included in the analysis)
N= 6345 adult patients (2312 cardiac failure patients ; 753 CPR patients; 3280 respiratory patients)
Age: adults cases
Patient selection: cardiac cases defined as those in whom primary reason for ECMO was cardiac dysfunction (including primary cardiomyopathies, myocarditis and postoperative cardiac surgical cases).
Technique: veno arterial ECMO (in more than 95% of patients)
Conflict of interest/source of funding: none</td>
<td>Number of patients analysed: varied by outcome
Survival to discharge or transfer (adults):
Cardiac cases: 39% (891/2312)
CPR: 27% (207/753)

Survival to discharge or transfer- by diagnosis in (age group >16 years)
<table>
<tr><th></th><th>% (n) survived</th></tr>
<tr><td>Congenital Defect</td><td>33(59)</td></tr>
<tr><td>Cardiogenic Shock</td><td>35(132)</td></tr>
<tr><td>Cardiomyopathy</td><td>46(132)</td></tr>
<tr><td>Myocarditis</td><td>66(57)</td></tr>
<tr><td>Other</td><td>38(577)</td></tr>
</table>
</td>
<td>Mechanical and patient-related complications for the cardiac population (>16 years)
<table>
<tr><th>Mechanical</th><th>% reported (% survival)</th></tr>
<tr><td>Oxygenator failure</td><td>15.1(36)</td></tr>
<tr><td>Cannula problems</td><td>4.4(27)</td></tr>
<tr><td>Pump malfunction</td><td>0.7(28)</td></tr>
<tr><td>Tubing rupture</td><td>0.2(0)</td></tr>
<tr><td></td><td></td></tr>
<tr><td>Patient-related</td><td></td></tr>
<tr><td>Surgical site bleeding</td><td>25.5(34)</td></tr>
<tr><td>Cannula site bleeding</td><td>20.9(39)</td></tr>
<tr><td>Cardiac tamponade</td><td>5.7(27)</td></tr>
<tr><td>Clinical seizures</td><td>2.1(15)</td></tr>
<tr><td>Intracranial haemorrhage</td><td>1.7(7)</td></tr>
</table>
</td>
<td>Study design issues:
• Registry report on neonatal, paediatric and adult cases of use of ECMO for respiratory extracorporeal CPR, or cardiac cases (n=50,667). Results for adult cardiac and CPR cases are reported here.
• Data from 170 centres in 2011.
• Authors note that 2012 data are underrepresented because of delays in reporting to the register.
• A complication was recorded as such if it required active management such as equipment change, change in therapy or resulted in organ dysfunction.
• For cardiac cases, adult population defined as >16 years.</td>
</tr>
</table>

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Study details

Combes A (2008)[5]

Case series

France

Recruitment period: 2003-6

Study population: patients who received ECMO during ICU stay. Reasons for ECMO support: DCM (22%); acute myocardial infarction, fulminant myocarditis, PCCS (20% each); post transplantation cardiac graft failure (12%) and miscellaneous (including accidental injury) (6%).

n = **81**

Age: mean 46 years

Sex: 57% male

Patient selection criteria: Patients with signs of acute refractory cardiogenic shock were included.

Key efficacy findings

Number of patients analysed: **81**

Survival to discharge: 42% (34/81);

28-day survival: 48%; **90-day survival**: 38%

(numbers not reported)

Long-term survivors: 36% (29/81)

Outcomes	Survivors (n=34)	Nonsurvivors (n=47)	p
Days, median (IQR)			
ECMO duration	7(5-10)	4(1-12)	0.04
ICU stay	21(12-31)	4(2-15)	<0.0001
Mechanical ventilation duration	17(8-25)	3(2-10)	0.0002
%(n)			
Patients on Mechanical ventilation	88(30)	100(47)	0.03
Bridge to VAD after ECMO	15(5)	2(1)	0.03
Bridge to heart transplant after ECMO	21(7)	4(2)	0.03
SOFA scores; mean (SD)			
At time of ECMO implantation	13(5)	16(5)	0.007
Day 3	12(5)	17(4)	<0.0001
Day 7	10(5)	7(6)	<0.0001

Key safety findings

Death (n) (was 'mainly ' because of refractory MOF; 14 died within 24 hours)

	Under ECMO support; n=38	After weaning; n=9	After ICU discharge[a] n=5
DCM (18)	11	2	1
Acute myocardial infarction (16)	10	1	0
Fulminant myocarditis (16)	6	0	1
PCCS(16)	5	3	1
Transplant(10)	3	2	2
Other (5)	3	1	0

[a]1 to 5 months after discharge

Overall major complications: 65% (22) for survivors and 51% (24) for non survivors (p=0.27).

	Survivors (n=34)	Nonsurvivors (n=47)
Major bleeding	35(12)	30(14)
Femoral vein thrombosis[a]	18(6)	4(2)
Arterial ischaemia	24(8)	15(7)
Vena cava thrombosis	12(4)	4(2)
Surgical wound infection	18(6)	17(8)
Overt pulmonary oedema	3(1)	9(4)
Stroke	12(4)	6(3)

Comments

Follow-up issues:

- 1 patient lost to follow- up.

Study design issues:

- Retrospective review of patients consecutively enrolled in a single centre
- SOFA score assesses extent of organ function or rate of failure and is based on different scores for the respiratory, cardiovascular, hepatic, coagulation, renal and neurological systems; total scores range from 0-24, higher score indicating greater organ dysfunction/failure.
- In the multivariate logistic regression analysis, factors with p≤0.10 in univariate analysis were included.

Study population issues:

- Patients had

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<table>
<tr><th>Study details</th><th>Key efficacy findings</th><th>Key safety findings</th><th>Comments</th></tr>
<tr>
<td>Patients receiving venovenous ECMO were excluded.

Technique: ECMO used (oxygenator: Quadrox Bioline, Jostra-Maquet), and a centrifugal pump (Rotaflow, Jostra-Maquet). Cannulation either via femoral vessels (74%) or central right atrial and aortic cannulae (Biomedicus Carmeda, Medtronic).

Follow-up: median 11 months.

Conflict of interest/source of funding: none</td>
<td>HRQoL (n=28)- by median duration of follow-up; mean (SD)
<table>
<tr><th>SF-36 domain</th><th><325 days (n=14)</th><th>≥ 325 days (n=14)</th><th>p</th></tr>
<tr><td>Physical component</td><td>40(11)</td><td>53(4)</td><td>0.0001</td></tr>
<tr><td>Mental component</td><td>44(10)</td><td>48(9)</td><td>0.34</td></tr>
<tr><td>General health</td><td>50(21)</td><td>72(17)</td><td>0.01</td></tr>
<tr><td>Vitality</td><td>57(31)</td><td>80(13)</td><td>0.02</td></tr>
</table>
The scores were compared against other patient groups including age and sex-matched controls and patients with NYHA class III heart failure.

In comparison to age- and sex-matched controls, HRQoL was impaired for physical health and social function while vitality and mental health were deemed ‘satisfactory’. HRQoL was considered to be ‘significantly’ better than those of NYHA class III patients and ‘comparable’ to NYHA class I patients. Numbers not reported for these comparative groups.</td>
<td>
<table>
<tr><td>Renal replacement therapy[b]</td><td>38(13)</td><td>77(36)</td></tr>
</table>
[a]p=0.06; [b]p=0.03

Additional infections:
Ventilator-associated pneumonia (n=40; 1or more episode), bacteraemia (n=11) and catheter-related infections (n=5) were reported.
Additional events;
Persistent problems at cannula-insertion site (lymphocele, late wound healing) was reported in 4 patients, femoral artery aneurysm needing surgical repair in 1 patient, symptoms related to crural nerve injury (skin numbness and/or paraesthesia) was reported in 9 patients who had femoral ECMO.

Early independent predictors of ICU deaths were :

sex (female) (OR 3.9 [95% CI 1.1 to 14.2]; p=0.04);
myocarditis (OR 0.1 [95%CI 0.02 to 0.78); p=0.03);
ECMO under CPR (OR 20.7 [95%CI1.1 to 392.0]; p=0.04);
prothrombin activity <50% (OR 3.9 [1.1to13.9]; p=0.03); and
24 hour urine output <500ml (OR 6.5 [95% CI 1.9 to 22.7]; p=0.003).

</td>
<td>undergone percutaneous coronary intervention or IABP before ECMO.

Other issues:

Scores for all SF-36 domains that concern physical health (physical functioning, role-physical, bodily pain) and mental health (social functioning, role-emotional, mental health) were reported in text. Only the key scores reported in this table.
There appears to be some discrepancy between the numbers reported, graphical presentation and text on scores for vitality and social functioning.

</td>
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</table>

Abbreviations used: AM, acute myocarditis; ARDS, acute respiratory distress syndrome; AVR, aortic valve replacement; CABG, coronary artery bypass graft; CBP, cardiopulmonary bypass; CPR, cardiopulmonary resuscitation; DIC, disseminated intravascular coagulation; DCM, dilated cardiomyopathy; HF, heart failure; ICU, intensive care unit; HRQoL, health related quality of life; IABP, intra-aortic balloon pump; IQR, interquartile range; IV, intravenous; MOF, multiple organ failure; NYHA, New York Heart Association functional classification; OR, odds ratio; PCCS, postcardiotomy cardiogenic shock; SOFA, Sequential Organ Failure Assessment score; VAD, ventricular assist device.

Study details	Key efficacy findings	Key safety findings	Comments

Chung JC(2010)[6]
 	
Case series
Taiwan
Recruitment period: 1995-2007
Study population: acute circulatory collapse
n = **70**
Age: mean 46 years
Sex: 79% male
 	
Patient selection criteria: ECMO after circulatory collapse with an intent to bridge to heart transplant.
 	
Technique: Femoral veno arterial ECMO. Patients switched to BiVAD if evidence of right heart dysfunction
 	
Follow-up: **1 year**
 	
Conflict of interest/source of funding:
not reported
	Number of patients analysed: **70**
	Outcomes:
	• Successfully bridged to heart transplant or VAD: 44% (31/70) [duration of ECMO median 140 hours].
	  ○ Bridged to VAD: n=16 (after duration of median150 hours on ECMO)
	  ○ Direct bridge to heart transplant: n=15 (after duration of median 120 hours on ECMO)
	• Unsuccessfully bridged: 56%(39/70); duration of ECMO median 70 hours.
	  ○ 1 patient was in a vegetative stage after ECMO removal
	  ○ 1 patient underwent implantation of cardioverter defibrillator
	  ○ Remaining 37 patients died
	
	• Overall hospital survival rate for all ECMO patients with an initial intent to bridge to heart transplant: 27% (19/70)
	
	Of the patients who were directly bridged to heart transplant (n=15)
	• Survived: n=11 (100% 1-year survival rate)
	
	Of the patients who were bridged to VAD (n=16)
	• Bridged to heart transplant and discharged: n=8 (100% 1-year survival rate)
	
	Independent factors related to unsuccessful bridging (multivariate logistic regression):
	Factors: OR (95% CI);p
	Age > 50 years: 8.3 (2.1 to 33.3); p=0.003
	Pre-ECMO CPR: 12.3(2.9 to 52.6); p=0.001
	SOFA score >10: 5.3 (1.3 to 21.3); p=0.02
		Death
		In patients not successfully bridged (n=39) (on ECMO for median 70 hours):
		• died on ECMO: 62% (24/39)
		• died in-hospital after removal of ECMO: 33% (13/39)
		In patients directly bridged to heart transplant (n=15):
		• died: 27% (4/15)
		In patients bridged to VAD (n=16):
		• died on VAD: 50% (8/16)
		
		Dialysis
		Patients successfully bridged (n=31) %(n) / Patients unsuccessfully bridged (n=39) %(n)
		Before ECMO: 0 / 8(3)
		During ECMO[a]: 19%(6) / 33%(13)
		[a]p=0.09
			Study design issues:
			• Retrospective review.
			• SOFA score: range from 0-24, higher score indicating greater organ dysfunction/failure.
			• In the multivariate logistic regression analysis, factors with p<0.10 in univariate analysis were included.
			Study population issues:
			• 13 patients excluded as <18 years.
			• Aetiology: DCM (39%), ischaemic cardiomyopathy (41%) and other (20%)
			• 53% (37/70) were on ECMO because of CPR.47% (33/70) were originally awaiting heart transplant.

Abbreviations used: AM, acute myocarditis; ARDS, acute respiratory distress syndrome; AVR, aortic valve replacement; CABG, coronary artery bypass graft; CBP, cardiopulmonary bypass; CPR, cardiopulmonary resuscitation; DIC, disseminated intravascular coagulation; DCM, dilated cardiomyopathy; HF, heart failure; ICU, intensive care unit; HRQoL, health related quality of life; IABP, intra-aortic balloon pump; IQR, interquartile range; IV, intravenous; MOF, multiple organ failure; NYHA, New York Heart Association functional classification; OR, odds ratio; PCCS, postcardiotomy cardiogenic shock; SOFA, Sequential Organ Failure Assessment score; VAD, ventricular assist device.

Study details

Belle L (2012)[7]

Case series

France

Recruitment period: 2006-10

Study population: patients with severe cardiogenic shock (27) and refractory cardiac arrest (24) (17 with out-of-hospital cardiac arrest; 7 with in-hospital cardiac arrest)

n = **51**

Age: mean 51 years

Sex: 75% male

Patient selection criteria: patients ≥18 years, refractory cardiac arrest or severe cardiogenic shock at risk of early death. Exclusion factors include: advanced age, terminal malignancy, and previous irreversible brain

Key efficacy findings

Number of patients analysed: **51**

Survival to hospital discharge: 27%(14/51)

Outcome	Cardiogenic shock (n=27) %(n)	Refractory cardiac arrest (n=24) %(n)
Implantation success[a]	96.3 (26)	75.0 (18)
Discharged alive and in a good neurological condition (all alive after a median of 17 months)	48.1 (13)	4.2 (1)
Heart transplant	3.7 (1)	0

[a]p=0.04;

Key safety findings

	Cardiogenic shock (n=27) %(n)	Refractory cardiac arrest (n=24) %(n)
Implantation failure	1 (3.7) (because of catheterisation failure)	6 (25.0) (because of catheterisation failure in 5 patients and centrifugal pump failure in 1 patient)
Death:		
in-hospital (23 in first 24 hours)	51.9 (14)	95.8 (23)
• under ECMO	37.0 (10)	70.8 (17)
• after failure of implantation	3.7 (1)	25.0(6)
• after ECMO weaning before discharge	11.1(3)	0
In-hospital complications		
Major bleeding [a]	44.4 (12)	33.3 (8)
Thrombocytopenia	44.4 (12)	25.0 (6)
Blood transfusion needed	29.6 (8)	20.8 (5)
DIC	22.2 (6)	20.8 (5)
Acute or sub-acute lower limb ischaemia[b]	18.5 (5)	16.7 (4)
Sepsis	22.2 (6)	4.2 (1)
Haemolysis	11.1 (3)	16.7 (4)
Intervention for major bleeding (no further details)	11.1 (3)	8.3 (2)
Haemofiltration needed for renal failure	14.8 (4)	0
Deep vein thrombosis	14.8 (4)	0
Stroke	3.7 (1)	4.2 (1)
Major primary causes of in-hospital death		
MOF	29.6 (8)	33.3 (8)
Implantation failure	3.7 (1)	25.0 (6)
Haemorrhagic shock	11.1 (3)	8.3 (2)
Intra-cardiac thrombus	7.4 (2)	0

Comments

Study design issues:

- Prospective study with consecutively enrolled patients.

Study population issues:

- Cardiac arrest was defined as no spontaneous circulation after 30 minutes of CPR.
- Severe cardiogenic shock was defined as systolic blood pressure <90 mmHg despite treatment with high-dose catecholamine (inotropic and vasopressor agents).
- Diagnosis: acute coronary syndrome, cardiomyopathy, drowning, cardiotoxicity, myocarditis, complication during catheterisation, pulmonary embolism, cardiac tamponade.
- 1 patient with ARDS included in

Abbreviations used: AM, acute myocarditis; ARDS, acute respiratory distress syndrome; AVR, aortic valve replacement; CABG, coronary artery bypass graft; CBP, cardiopulmonary bypass; CPR, cardiopulmonary resuscitation; DIC, disseminated intravascular coagulation; DCM, dilated cardiomyopathy; HF, heart failure; ICU, intensive care unit; HRQoL, health related quality of life; IABP, intra-aortic balloon pump; IQR, interquartile range; IV, intravenous; MOF, multiple organ failure; NYHA, New York Heart Association functional classification; OR, odds ratio; PCCS, postcardiotomy cardiogenic shock; SOFA, Sequential Organ Failure Assessment score; VAD, ventricular assist device.

Study details	Key efficacy findings	Key safety findings	Comments
damage. Technique: ECMO(bypass: Biomedicus, Medtronic; oxygenator: Jostra-Maquet) via a percutaneous femoral approach. IABP inserted before ECMO were left in place. ECMO implanted at home in 1 patient. Follow-up: **median 17 months** Conflict of interest/source of funding: none		Brain death 0 8.3 (2) Haemorrhagic stroke 0 4.2 (1) DIC 0 4.2 (1) Cardiac rupture 0 4.2 (1) Unknown or undefined 0 8.3 (2) [a]defined as a blood loss needing transfusion, reintervention or resulting in death; [b]1 needed surgery none underwent amputation.	the cardiogenic shock population.

Abbreviations used: AM, acute myocarditis; ARDS, acute respiratory distress syndrome; AVR, aortic valve replacement; CABG, coronary artery bypass graft; CBP, cardiopulmonary bypass; CPR, cardiopulmonary resuscitation; DIC, disseminated intravascular coagulation; DCM, dilated cardiomyopathy; HF, heart failure; ICU, intensive care unit; HRQoL, health related quality of life; IABP, intra-aortic balloon pump; IQR, interquartile range; IV, intravenous; MOF, multiple organ failure; NYHA, New York Heart Association functional classification; OR, odds ratio; PCCS, postcardiotomy cardiogenic shock; SOFA, Sequential Organ Failure Assessment score; VAD, ventricular assist device.

Study details

Unosawa S (2013)[8]
Case series
Japan
Recruitment period: 1992-2007
Study population: patients with refractory PCCS
n = **47**
Age: mean 64 years
Sex: 74% male
Patient selection criteria: systemic perfusion low despite high-dose inotropic agents and/or IABP.
Technique: Heparin coated ECMO (centrifugal blood pump: Capiox HP, Terumo and membrane oxygenator, Terumo) inserted either into the femoral artery (68%) or ascending aorta.
ECMO instituted in operating room (70%) or ICU (30%). IABP used in 83%.

Key efficacy findings

Number of patients analysed: **47**

Outcomes	
Duration of ECMO Mean (range)	63.5 hours (9-336)
Patients weaned off ECMO ;%(n)	62% (29/47)
Survival to discharge %(n)	30% (14/47)
Overall survival rates of patients who were discharged from hospital (%):	
3 years	84.4
5 years	67.5
10 years	59.1
Cumulative survival rates (%) :	
7 days	57.5
30 days	34.0
3 months	31.9
1 year	29.8
3 years	27.7
5 years	20.1
10 years	17.6

Of the 14 patients survived to discharge, 7 were alive at 'long-term' follow-up (6 in NYHA class I or II; 1 bedridden).

There was no case of bridging to heart transplantation or VAD.

Key safety findings

Overall in-hospital mortality: 70%(33/47)
- during ECMO support: 38% (18/47)
- after weaned off from ECMO: 52% (15/29) (mean period from weaning off ECMO to death was 18 days [range 1 to 118]).
  - Multivariate analysis: ECMO support for >48 hours (OR 8.9 95% CI 1.3 to 62.9; p=0.03) was a significant predictor of mortality in patients weaned off ECMO.

Cause of death:	Died during ECMO (n=18)	Died after ECMO (n=15)
HF	7	2
MOF	5	8
Brain death	4	2
Severe coagulopathic bleeding	2	-
Cardiac rupture	-	2
Pneumonia	-	1

7 patients died during the follow-up: 2 of cardiac events and 5 of non-cardiac causes including a ruptured iliac artery aneurysm, subarachnoid haemorrhage, pneumonia, heat stroke and an unknown cause.

Other complications:	Died during ECMO (n=18)	Died after ECMO (n=15)	Survivors (n=14)
Leg ischaemia	7	1	4
Dialysis for acute renal failure	7	7	1
Pneumonia	-	5	1
Wound infection	-	2	6
Rethorax (not defined)	13	11	9

Comments

Study design issues:
- Actuarial survival rates calculated using Kaplan-Meier.
- For multivariate analysis, only variables with p<0.01 in the univariate analysis included into the logistic regression model.

Study population issues:
- Types of operation: CABG (40%), valve surgery (17%); aortic surgery, post-infarction ventricular septal defect closure (12% each), concomitant aortic surgery and CABG (6%), concomitant valve surgery and CABG, aortic root replacement and pulmonary embolectomy (4% each).

Abbreviations used: AM, acute myocarditis; ARDS, acute respiratory distress syndrome; AVR, aortic valve replacement; CABG, coronary artery bypass graft; CBP, cardiopulmonary bypass; CPR, cardiopulmonary resuscitation; DIC, disseminated intravascular coagulation; DCM, dilated cardiomyopathy; HF, heart failure; ICU, intensive care unit; HRQoL, health related quality of life; IABP, intra-aortic balloon pump; IQR, interquartile range; IV, intravenous; MOF, multiple organ failure; NYHA, New York Heart Association functional classification; OR, odds ratio; PCCS, postcardiotomy cardiogenic shock; SOFA, Sequential Organ Failure Assessment score; VAD, ventricular assist device.

Study details	Key efficacy findings	Key safety findings	Comments
Follow-up: **10 years** Conflict of interest/source of funding: none			

Abbreviations used: AM, acute myocarditis; ARDS, acute respiratory distress syndrome; AVR, aortic valve replacement; CABG, coronary artery bypass graft; CBP, cardiopulmonary bypass; CPR, cardiopulmonary resuscitation; DIC, disseminated intravascular coagulation; DCM, dilated cardiomyopathy; HF, heart failure; ICU, intensive care unit; HRQoL, health related quality of life; IABP, intra-aortic balloon pump; IQR, interquartile range; IV, intravenous; MOF, multiple organ failure; NYHA, New York Heart Association functional classification; OR, odds ratio; PCCS, postcardiotomy cardiogenic shock; SOFA, Sequential Organ Failure Assessment score; VAD, ventricular assist device.

Study details	Key efficacy findings	Key safety findings	Comments
Schwarz B (2003)[9] **Case series** (retrospective) Austria Study population: patients with cardiogenic shock (n=25) or prolonged cardiopulmonary arrest (n=21) Recruitment period: 1996-2001 n = **46** (adults and children) Age: mean 48 years Sex: 76% male Technique: venoarterial ECMO (Biodmedicus; Medtronic) Conflict of interest/source of funding: not reported	**Left ventricular distension** Left ventricular distension and pulmonary oedema as a result of transient left ventricular unloading was reported in 8% (2/25) of patients with cardiogenic shock and 14 %(3/21) with cardiopulmonary arrest (timing unclear). All managed with inotropic support.		Study population: • Included adults and children (numbers for each group not reported). • Exclusion criteria*:* Patients with post bypass cardiogenic shock who received CBP after open heart surgery because of an inability to be weaned from extracorporeal circulation. • 1 patient (with cardiogenic shock) who had left ventricular distension was 14 years.
Kittleson MM (2011)[10] **Case series** USA Study population: patients receiving transplants for reasons including idiopathic or	**Pseudoaneurysm** Pseudoaneurysm was reported in 1 patient for whom ECMO was used as pre-emptive therapy.		ECMO used as pre-emptive therapy in 19 patients and as salvage therapy in 14 patients in heart transplant recipients with severe rejection and refractory cardiogenic shock.

Abbreviations used: AM, acute myocarditis; ARDS, acute respiratory distress syndrome; AVR, aortic valve replacement; CABG, coronary artery bypass graft; CBP, cardiopulmonary bypass; CPR, cardiopulmonary resuscitation; DIC, disseminated intravascular coagulation; DCM, dilated cardiomyopathy; HF, heart failure; ICU, intensive care unit; HRQoL, health related quality of life; IABP, intra-aortic balloon pump; IQR, interquartile range; IV, intravenous; MOF, multiple organ failure; NYHA, New York Heart Association functional classification; OR, odds ratio; PCCS, postcardiotomy cardiogenic shock; SOFA, Sequential Organ Failure Assessment score; VAD, ventricular assist device.

Study details	Key efficacy findings	Key safety findings	Comments
ischaemic cardiomyopathy Recruitment period: 1997-2009 n = **32** Age: mean 48 years Sex: 64% male Technique: ECMO for pre-emptive or salvage therapy. Conflict of interest/source of funding: none			
Leontiadis (2010)[11] **Case report** Germany Study population: patient with refractory cardiogenic shock after percutaneous coronary intervention Recruitment period: not reported n = **1** Age: 58 years Sex: male Technique: ECMO and IABP Conflict of	**Aortic root thrombosis** Patient with known coronary artery disease and moderate left ventricular dysfunction presented with an acute coronary syndrome. Patient developed cardiogenic shock after percutaneous coronary intervention and was supported with ECMO and IABP. Massive thrombus of the aortic root and ascending aorta was reported in the patient while undergoing evaluation for implantation of a VAD as a bridge to transplantation. Patient was treated by anticoagulants and subsequently died 24 hours later because of MOF.		

Abbreviations used: AM, acute myocarditis; ARDS, acute respiratory distress syndrome; AVR, aortic valve replacement; CABG, coronary artery bypass graft; CBP, cardiopulmonary bypass; CPR, cardiopulmonary resuscitation; DIC, disseminated intravascular coagulation; DCM, dilated cardiomyopathy; HF, heart failure; ICU, intensive care unit; HRQoL, health related quality of life; IABP, intra-aortic balloon pump; IQR, interquartile range; IV, intravenous; MOF, multiple organ failure; NYHA, New York Heart Association functional classification; OR, odds ratio; PCCS, postcardiotomy cardiogenic shock; SOFA, Sequential Organ Failure Assessment score; VAD, ventricular assist device.

Study details	Key efficacy findings	Key safety findings	Comments
interest/source of funding: not reported			

Efficacy

Survival to discharge

A register including 3065 adult cardiac failure and cardiopulmonary resuscitation (CPR) patients reported survival to discharge or transfer in 39% (891/2312) of cardiac failure patients and 27% (207/753) of CPR patients[4].

Four case series of 81 patients (with acute refractory cardiogenic shock), 295 patients (treated by ECMO supported CPR), 219 patients (with refractory postcardiotomy cardiogenic shock) and 24 patients (with refractory cardiac arrest included in a case series of 51 patients) reported survival to discharge in 42% (34/81), 27% (79/295), 24% (52/219) and 4% (1/24) of patients respectively[5,3,1,7].

Overall survival

The case series of 219 patients reported overall survival of 17% (37/219) (74% [37/50] for those who were discharged) at 5-year follow-up[1].

A case series of 47 patients with refractory postcardiotomy cardiogenic shock who were discharged from hospital after ECMO reported an overall survival rate of 59% at 10 years[8].

Duration of mechanical ventilation

The case series of 219 patients reported that the mean duration of mechanical ventilation was 12 days[1].

Quality of life

The case series of 81 patients (28 patients available for quality of life evaluation) reported a significant difference in physical component (p=0.0001), general health (p=0.01) and vitality (p=0.02) domains of SF-36 quality of life scores in 14 patients who were followed-up for a longer time period (325 days or more) compared with patients followed up for fewer than 325 days (n=14) (higher scores in patients followed up for 325 days or more). There was no significant difference in the mental component scores. The same study compared scores with age- and sex-matched controls and reported physical health and social function domains were ‘impaired’ for the group treated by ECMO but vitality and mental health were ‘satisfactory’[5].

Bridge to device or transplant

The case series of 219 patients reported that 4% (8/219) of patients were bridged to a long-term ventricular assist device. Five patients subsequently died, 2 had a success transplant and 1 was successfully weaned from ECMO[1].

A case series of 131 patients with cardiogenic shock reported 21% (28/131) of patients were bridged to a ventricular assist device. Three patients were subsequently weaned from the device (bridge to recovery) and 11 patients were bridged to heart transplant[2].

A case series of 70 patients with acute circulatory collapse reported 44% (31/70) of patients were successful bridged to a ventricular assist device (n=16) or directly bridged to heart transplant (n=15). Of the patients bridged to a ventricular assist device, 50% (8/16) were bridged to heart transplant and discharged, and the remaining patients died while on a ventricular assist device. Of the patients who were directly bridged to heart transplant, 4 patients subsequently died. Fifty-six percent (39/70) were unsuccessfully bridged (37 patients died; 1 patient underwent an implantation of cardioverter defibrillator and 1 patient was in a vegetative stage after ECMO removal) [6].

The case series of 81 patients with acute refractory cardiogenic shock reported bridge to heart transplantation after ECMO in 11% (9/81) of patients and bridge to ventricular assist device in 7% (6/81) of patients[5].

Safety

Death

Death during ECMO support was reported in 40% (52/131) of patients in the case series of 131 patients; in 'most cases' this was because of multi-organ failure or sepsis[2].

Death within 30 days was reported in 76% (167/219) of patients in the case series of 219 patients with refractory postcardiotomy cardiogenic shock; the main cause of death was low cardiac output syndrome secondary to refractory myocardial failure (71%)[1].

Death on ECMO was reported in 62% (24/39) of patients who were not successfully bridged and 33% (13/39) died in hospital after removal of ECMO in the case series of 70 patients[6]. Death in hospital was reported in 52% (14/27) of patients with severe cardiogenic shock and 96% (23/24) of patients with refractory cardiac arrest in the case series of 51 patients[7].

Haemorrhage

Intracranial haemorrhage was reported in 2% of patients in the register reporting on 2312 cardiac patients (absolute numbers not reported; timing unclear)[4].

Cerebral haemorrhage was reported in 5% (11/219) of patients in the case series of 219 patients[1].

Coagulopathy

Disseminated intravascular coagulation was reported in 22% (6/27) of patients with severe cardiogenic shock and 21% (5/24) of patients with refractory cardiac arrest (cause of death in 1 patient) in the case series of 51 patients (timing unclear)[7].

Stroke

Stroke was reported in 9% (7/81) of patients in the case series of 81 patients (timing unclear)[5]. Stroke was reported in 1 patient with severe cardiogenic shock and 1 patient with refractory cardiac arrest in the case series of 51 patients (timing unclear)[7].

Perforation

Femoral artery perforation (leading to uncontrollable bleeding and subsequent death) was reported in 2 patients in the case series of 131 patients[2].

Lower limb ischaemia

Lower limb ischaemia was reported in 13% (28/219) of patients in the case series of 219 patients; fasciotomy for severe leg ischaemia was needed in 6% (13/219) of patients (timing unclear)[1].

Deep vein thrombosis

Deep vein thrombosis (during hospitalisation) was reported in 15% (4/27) of the 27 patients with severe cardiogenic shock in the case series of 51 patients[7].

Pseudoaneurysm

Pseudoaneurysm was reported in 1 patient in a case series of 32 patients[10].

Left ventricular distension

Left ventricular distension was reported in 8% (2/25) of patients with cardiogenic shock and 14% (3/21) of patients with cardiopulmonary arrest in a case series of 46 patients (timing unclear)[9].

Infection

Ventilator-associated pneumonia (1 or more episode) was reported in 49% (40/81) of patients, surgical wound infections in 17% (14/81) of patients, bacteraemia in 14% (11/81) of patients, and catheter-related infections in 6% (5/81) of patients in the case series of 81 patients (timing unclear)[5].

Mechanical problems

Mechanical complications including oxygenator failure (15%; 36% of these patients survived), cannula problems (4%; 27% survived) and tubing rupture (less than 1%; none survived) and pump malfunction (less than 1%; 28% survived) were reported in cardiac patients (n=2312) included in the register of patients treated by ECMO (absolute numbers not reported) [4].

Clots in the ECMO circuit were reported in 19% (56/295) of patients and air embolus in 2% (5/295) of patients in the case series of 295 patients [3].

Validity and generalisability of the studies

- Studies included in table 2 are from mainly case series. No randomised controlled trials were identified.
- Studies evaluating use of ECMO in adult populations have been selected for presentation (but 2 studies[2,9] included both children and adults). We have been advised by specialist advisers that it would be appropriate to produce a separate guidance on ECMO for acute heart failure in children.
- The literature includes studies of ECMO use for diverse indications. For the purpose of this review, studies of ECMO use for the following main indications have been selected; postcardiotomy cardiogenic shock, cardiomyopathy, cardiac arrest or following cardiopulmonary resuscitation.
- ECMO was instituted in an operating room, intensive care unit or at home. Specialist advisers have noted that ECMO kits have evolved and portable ECMO may be used outside of the hospital setting.
- Data from the Extracorporeal Life Support Organization register were reported in 2 studies[3,4].

Existing assessments of this procedure

There were no published assessments from other organisations identified at the time of the literature search.

Related NICE guidance

Below is a list of NICE guidance related to this procedure. Appendix B gives details of the recommendations made in each piece of guidance listed.

Interventional procedures

- Extracorporeal membrane oxygenation for severe acute respiratory failure in adults. NICE interventional procedure guidance 391 (2011). Available from www.nice.org.uk/guidance/IPG391
- Short-term circulatory support with left ventricular assist devices as a bridge to cardiac transplantation or recovery. NICE interventional procedure guidance 177 (2006). Available from www.nice.org.uk/guidance/IPG177
- Extracorporeal membrane oxygenation (ECMO) in post neonatal children. NICE interventional procedure guidance 38 (2004). Available from www.nice.org.uk/guidance/IPG38

Specialist advisers' opinions

Specialist advice was sought from consultants who have been nominated or ratified by their specialist society or royal college. The advice received is their individual opinion and does not represent the view of the society.

Dr Nick Banner, Dr Guy MacGowan (British Society of Heart Failure); Dr Jeremy Cordingley (Faculty of Intensive Care Medicine); Dr Nicholas Barrett, Dr Julian Barker (Intensive Care Society); Mr Giles Peek, Dr Jayan Parameshwar (Society for Cardiothoracic Surgeons in Great Britain and Ireland)

- One specialist adviser has performed this procedure regularly, 2 specialist advisers have performed this procedure at least once, and 2 specialist advisers have never performed this procedure. Two specialist advisers did not state their experience.
- All specialist advisers considered the procedure as definitely novel and of uncertain safety and efficacy and that fewer than 10% of specialists are engaged in this area of work.
- Comparators: standard ICU care, inotropic drugs, intra-aortic balloon pump, mechanical ventilation and mechanical circulatory support.
- Key efficacy outcomes: survival (hospital discharge; 28 days; 6 months (without severe disability); definitive therapy; long-term; neurologically intact), successful bridge to recovery (removal of device)or bridge to transplant or to

long-term ventricular assist device, functional capacity following support , and long- term quality of life.

- Adverse events reported in literature: bleeding, cannulation-related (misplacement, arterial rupture, bleeding, distal limb ischaemia, infection), intracerebral haemorrhage, neurological complications (anoxic, haemorrhagic, thrombotic central nervous system) circuit-related complications (air embolus, haemolysis, thrombosis, failure),oxygenator failure needing exchange, coagulopathy, left ventricular distension, aortic root thrombosis, stroke, failure to decompress left atrium with pulmonary oedema, renal failure, sepsis, multiorgan failure and death.
- Anecdotal adverse events: false aneurysm, intrathoracic bleeding and tamponade, left ventricular thrombus formation and/or acute pulmonary injury, difficulty with cerebral oxygenation, embolism and systemic inflammatory response syndrome.
- If the procedure is safe and efficacious, 5 specialist advisers stated that it is likely to be carried out in a minority of hospitals (at least 10 in the UK) and 2 stated fewer than 10 specialist centres.
- In terms of numbers of patients eligible for treatment and use of resources, 3 specialist advisers stated that the potential impact of this procedure on the NHS would be major,1 stated it would be moderate and 3 stated that it would be minor.

Patient commentators' opinions

NICE's Public Involvement Programme was unable to gather patient commentary for this procedure.

Issues for consideration by IPAC

- Studies have been restricted to adult populations.
- One specialist adviser has suggested the title: ECMO for adults with acute heart failure

- Ongoing trials:
  - NCT01298050 Refractory in and out of hospital cardiac arrest treated with extracorporeal membrane oxygenation. Type: case series; location: Italy; estimated enrolment: 40; study start date: July 2011; estimated study completion date: July 2013.
  - NCT01605409 Emergency cardiopulmonary bypass after cardiac arrest with ongoing cardiopulmonary resuscitation. Type: randomised controlled trial. location: Austria; estimated enrolment: 40; study start date: September 2012; estimated study completion date: December 2014.
  - NCT01551849 Echocardiographic assessment of cardiac function during ECMO support. Type: case series; location: USA; estimated enrolment: 24; study start date: January 2012; estimated study completion date: December 2014.
  - NCT01186614 Refractory out-of-hospital cardiac arrest treated with mechanical CPR, hypothermia, ECMO and early reperfusion (CHEER). Type: case series; location: Australia; estimated enrolment: 24; study start date: November 2010; estimated study completion date: December 2013.
  - NCT00425685 Use of extracorporeal membrane oxygenationin treatment of acute myocaridal infarction following cardiac surgery procedures. Type: case series; location: Germany; estimated enrolment: 60; study start date: January 2003; estimated study completion date: December 2006.
- The following trial highlighted by a specialist adviser has been noted as having been completed:
  - NCT00173615 Extracorporeal membrane oxygenation effect in prolonged cardiopulmonary resuscitation. Type: case series; estimated enrolment: 100; location: Taiwan; study completion date: December 2006.

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Appendix A: Additional papers on extracorporeal membrane oxygenation (ECMO) for acute heart failure in adults

The following table outlines the studies that are considered potentially relevant to the overview but were not included in the main data extraction table (table 2). It is by no means an exhaustive list of potentially relevant studies.

Due to the high volume of relevant papers identified, a threshold for inclusion in Appendix A was set. Only relevant papers reporting on more than 40 patients have been included, unless they report on important safety events not described in Table 2.

Article	Number of patients/follow-up	Direction of conclusions	Reasons for non-inclusion in table 2
Aissaoui N, Luyt CE, Leprince P et al. (2011) Predictors of successful extracorporeal membrane oxygenation (ECMO) weaning after assistance for refractory cardiogenic shock. Intensive Care Medicine 37:1738-45.	N= 51 Follow up= unclear	Patients who tolerated a full ECMO weaning trial and had aortic VTI ≥10 cm, LVEF >20-25%, and TDSa ≥6 cm/s at minimal ECMO flow were all successfully weaned	Reports results for doppler echocardiography parameters as predictors of subsequent ECMO weaning success in patients recovering from severe cardiogenic shock
Bakhtiary F, Keller H, Dogan S et al. (2008) Venoarterial extracorporeal membrane oxygenation for treatment of cardiogenic shock: clinical experiences in 45 adult patients. Journal of Thoracic & Cardiovascular Surgery 135:382-88.	N= 45 Follow up= 3 years	Twenty-five patients could be successfully weaned from ECMO. The 30-day mortality was 53% (24/45 patients). The in-hospital mortality was 71% (32/45). Thirteen (29%) patients could be successfully discharged. After a follow-up period of up to 3 years, 22% (10) patients were still alive	Larger studies included in table 2.
Beurtheret S, Mordant P, Paoletti X et al. (2013) Emergency circulatory support in refractory cardiogenic shock patients in remote institutions: a pilot study (the cardiac-RESCUE program). European Heart Journal 34:112-20.	N= 87 Follow up= unclear	Independent predictors for in-hospital mortality included initiation of ECMO during cardiopulmonary resuscitation [hazard ratio (HR) = 4.81, 95% CI 2.25-10.30, P < 0.001] and oligo-anuria (HR = 2.48, 95% CI 1.29-4.76, P = 0.006).	Larger studies included in table 2.
Bisdas T, Beutel G, Warnecke G et al. (2011) Vascular complications in patients undergoing femoral cannulation for extracorporeal membrane oxygenation support. Annals of Thoracic Surgery 92:626-31.	N= 174 Follow up= unclear	Vascular complications were observed in 10% (17) of patients. Death within 30 days was 61%.	Larger studies included in table 2.
Chang WW, Tsai FC, Tsai TY et al. (2012) Predictors of mortality in patients successfully weaned from extracorporeal membrane oxygenation PLoS ONE [Electronic Resource] 7(8): e42687.	N=119 Follow-up= 6 months	Overall mortality rate was 26%. Multiple logistic regression analysis indicated that daily urine output on the second day of ECMO removal (UO24–48 hour), mean arterial pressure (MAP), and SOFA score on the day of ECMO removal were independent predictors	Larger studies included in table 2.

		of hospital mortality.	
Chen Y-S, Chao A, Yu H-Y et al. (2003) Analysis and results of prolonged resuscitation in cardiac arrest patients rescued by extracorporeal membrane oxygenation Journal of the American College of Cardiology 41(2):197-203	N= 57 Follow up= mean 49 months	Survival rate was 32%. Multi-organ failure was the major reason for mortality.	Larger studies included in table 2.
Chou NK, Chi NH, Wu IW et al. (2010) Extracorporeal membrane oxygenation to rescue cardiopulmonary failure after heart transplantation: a single-center experience. Transplantation Proceedings 42:943-945.	N= 366 (40 needing ECMO) Follow up=	Survival rate was 52.5%(21/40) and weaning rate was 72.5%(29/40). None of the patients receiving ECMO more than 4 days survived.	Larger studies included in table 2.
Chung SY, Sheu JJ, Lin YJ et al. (2012) Outcome of patients with profound cardiogenic shock after cardiopulmonary resuscitation and prompt extracorporeal membrane oxygenation support: A single-center observational study Circulation Journal 76:1385-92	N=134 Follow up= 30 days (survival)	In-hospital mortality was 57.5%. Sixty-eight patients (50.7%) were successfully weaned from ECMO and 57 (42.5%) were discharged alive.	Larger studies included in table 2.
Dalton HJ, Rycus PT, and Conrad SA. (2005) Update on extracorporeal life support 2004. Seminars in Perinatology 29:24-33.	N= 28,985 (474 cardiac and 132 CPR) Follow up=14 years	Overall survival in cardiac patients ranged from 33% to 43%.	Updated register report included in table 2.
Doll N, Fabricius A, Borger MA et al. (2003) Temporary extracorporeal membrane oxygenation in patients with refractory postoperative cardiogenic shock--a single center experience. Journal of Cardiac Surgery 18:512-18.	N= 95 Follow up=unclear	45%(45) of patients were successfully weaned from ECMO and overall hospital mortality for all ECMO patients was 71%. Complications included renal failure, bleeding needing mediastinal reexploration , of the lower limbs ischaemia, cerebral oedema , and cerebral haemorrhage.	Larger studies included in table 2.
Elsharkawy HA, Li L, Esa WAS et al (2010)	N=233	36% survival rate. History of cardiogenic	Studies with longer follow-up included in

Outcomes in patients who require venoarterial extracorporeal membrane oxygenation support after cardiac surgery Journal of Cardiothoracic and Vascular Anesthesia 24(6):946-51	Follow up= discharge	shock and younger age were associated with decreased hospital mortality.	table 2.
Formica AF, Avalli L, Colgrande L et al. (2010)Extracorporeal membrane oxygenation to support adult patients with cardiac failure: predictive factors of 30-day mortality. Interactive Cardiovascular & Thoracic Surgery 10 (5):721-6	N=42 Follow up= unclear	Sixteen patients were discharged with a survival rate of 38.1%.	Larger studies included in table 2.
Hsu PS, Chen JL, Hong GJ et al. (2010) Extracorporeal membrane oxygenation for refractory cardiogenic shock after cardiac surgery: predictors of early mortality and outcome from 51 adult patients. European Journal of Cardio-Thoracic Surgery 37:328-33.	N= 51 Follow up=1 year	53%(27) were successfully weaned and 10 died in hospital. At 1 year follow-up, 15 patients had survived.	Larger studies included in table 2.
Hsu KH, Chi NH, Yu HY et al. (2011) Extracorporeal membranous oxygenation support for acute fulminant myocarditis: analysis of a single center's experience. European Journal of Cardio-Thoracic Surgery 40:682-688.	N=75 (adults and paediatrics)	Survival to discharge was 64% (n = 48), 61% in adult group, and 70.8% in paediatric group. Six patients were later bridged to VAD but 3 died of multiple-organ failure. Three patients (4%) underwent heart transplantation and all of them survived to discharge.	Larger studies included in table 2.
Kagawa E, Dote K, Kato M et al. (2012) Should we emergently revasularize occluded coronaries for cardiac arrest?: rapid-response extracorporeal membrane oxygenation and intra-arrest percutaneous coronary intervention Circulation 126:1605-13	N=86 Follow up= 1 year	ECMO plus intra-arrest PCI is associated with improved outcomes. 50% were weaned off from ECMO and 30-day survival was 29%.	Larger studies included in table 2.
Ko WJ, Lin CY, Chen RJ et al. (2002) Extracorporeal	N= 76 Follow up=33 months	Two patients were bridged to heart transplantation and two	Larger studies included in table 2.

membrane oxygenation support for adult postcardiotomy cardiogenic shock. Annals of Thoracic Surgery 73:538-45.		bridged to ventricular assist devices. Thirty patients died on ECMO support, 22 patients were weaned off ECMO support but presented intra-hospital mortality. The cause of mortality included brain death (n = 1), sudden death (n = 4), and multiple organ failure (n = 17). Twenty patients were weaned off ECMO support and survived to hospital discharge	
Liden H, Wiklund L, Haraldsson A et al. (2009) Temporary circulatory support with extra corporeal membrane oxygenation in adults with refractory cardiogenic shock. Scandinavian Cardiovascular Journal 43:226-32.	N= 52 Follow up= 3 years	Twenty-six patients were weaned from ECMO. Early mortality for all patients was 48%. Mortality beyond 30 days was 5.8%, with no mortality in the non-cardiotomy group.	Larger studies included in table 2.
Luo XJ, Wang W, Hu SS et al. (2009) Extracorporeal membrane oxygenation for treatment of cardiac failure in adult patients. Interactive Cardiovascular & Thoracic Surgery 9:296-300.	N= 45 Follow up= mean 16 months	60%(27) were successfully weaned and 5 were bridged to heart transplantation. In-hospital mortality was 4%(19).	Larger studies included in table 2.
Magovern GJ, Jr. and Simpson KA. (1999) Extracorporeal membrane oxygenation for adult cardiac support: the Allegheny experience. Annals of Thoracic Surgery 68:655-61.	N= 82 Follow up=unclear	Survival in PCCS was 36% (20 /55), cardiac graft failure group was 50%(2/4) and no patient supported on ECMO for cardiac resuscitation survived	Larger studies included in table 2.
Mirabel M, Luyt CE, Leprince P et al. (2011) Outcomes, long-term quality of life, and psychologic assessment of fulminant myocarditis patients rescued by mechanical circulatory support. Critical Care Medicine 39:1029-35.	N=41 Median 525 days	Compared to age- and sex-matched controls, Short Form-36 evaluation of health-related quality of life revealed satisfactory mental health and vitality but persistent physical and psychosocial-related difficulties	Likely overlap of patients with Combes in T2.
Pokersnik JA, Buda T, Bashour CA et al. (2012) Have changes in ECMO	N=49 Follow up=unclear	Adverse events include stroke, renal failure and bleeding needing	Larger studies included in table 2.Compares different ECMO devices.

technology impacted outcomes in adult patients developing postcardiotomy cardiogenic shock? Journal of Cardiac Surgery 27:246-52.		reexploration.	
Schmidt M, Brechot N, Hariri S et al. (2012) Nosocomial infections in adult cardiogenic shock patients supported by venoarterial extracorporeal membrane oxygenation. Clinical Infectious Diseases 55:1633-41.	N=220 Follow up= unclear	Ventilator-associated pneumonia , bloodstream infections, cannula infections, and mediastinitis infections occurred in 55%, 18%, 10% and 11% of the patients, respectively	Retrospective review reporting on infections. Some outcomes identified in table 2.
Takayama H, Truby L, Koekort M et al. (2013) Clinical outcome of mechanical circulatory support for refractory cardiogenic shock in the current era. Journal of Heart & Lung Transplantation 32:106-11.	N=90 Follow up=1 year	Survival to hospital discharge was 49%. Multivariate analysis showed on-going CPR to be an independent risk factor for mortality (OR = 5.79, 95% CI 1.285 to 26.08, p = 0.022)	Larger studies included in table 2.
Urban M, Szarszoi O, Pirk J et al. (2013) What is the optimal mode of mechanical support in transplanted patients with acute graft failure? Interactive Cardiovascular & Thoracic Surgery 16:517-9.	N= 8 studies Follow up=unclear	Survival ranged from 40-74% in patients rescued with ECMO compared against 33-60% in patients supported by VAD.	Review comparing use of ECMO or VAD in patients with acute heart transplant failure.
Wang J, Han J, Jia Y et al. (2009) Early and intermediate results of rescue extracorporeal membrane oxygenation in adult cardiogenic shock. Annals of Thoracic Surgery 88:1897-1903.	N=62 Follow up= mean 2 years.	Mean quality of life scores were significantly lower in vitality and mental health domains among ECMO survivors compared to patients without ECMO support (chosen randomly from a database of adult cardiac surgery patients).	Larger studies included in table 2.
Wang SH, Saiki Y, Singh G et al. (2001) Successful bridge to cardiac transplantation using conventional cardiac assist devices - University of Alberta experience. Cardiovascular Engineering 6:12-5.	N=308 (73 supported with ECMO or VAD) Follow up=1 year	40.7%(11) were bridged to transplantation and 9 survived to hospital discharge.	Larger studies included in table 2.
Yu K, Long C, Hei F et al. (2011) Clinical	N=121	Complications include mechanical failure of	Study compares two different ECMO circuit

evaluation of two different extracorporeal membrane oxygenation systems: a single center report. Artificial Organs 35:733-7.	Follow up= unclear	ECMO circuit, neurological complication,and limb ischaemia.	systems. Complications reported in table 2.

Appendix B: Related NICE guidance for extracorporeal membrane oxygenation (ECMO) for acute heart failure in adults

Guidance	Recommendations
Interventional procedures	**Extracorporeal membrane oxygenation for severe acute respiratory failure in adults. NICE Interventional procedure guidance 391 (2011).** 1.1 Evidence on the safety of extracorporeal membrane oxygenation (ECMO) for severe acute respiratory failure in adults is adequate but shows that there is a risk of serious side effects. Evidence on its efficacy is inadequate to draw firm conclusions: data from the recent CESAR (Conventional ventilation or extracorporeal membrane oxygenation for severe adult respiratory failure) trial were difficult to interpret because different management strategies were applied among many different hospitals in the control group and a single centre was used for the ECMO treatment group. Therefore this procedure should only be used with special arrangements for clinical governance, consent and research. 1.2 Clinicians wishing to undertake ECMO for severe acute respiratory failure in adults should take the following actions. • Inform the clinical governance leads in their Trusts. • Whenever possible, ensure that patients and their carers understand the uncertainty about the procedure's efficacy and its risks and provide them with clear written information. In addition, the use of NICE's information for patients ('Understanding NICE guidance') is recommended (available from www.nice.org.uk/IPG391/publicinfo)

	1.3 Extracorporeal membrane oxygenation for severe acute respiratory failure in adults should only be carried out by clinical teams with specific training and expertise in the procedure. 1.4 Clinicians are encouraged to submit data on all adults undergoing ECMO for severe acute respiratory failure to the international Extracorporeal Life Support Organization register (www.elso.med.umich.edu). 1.5 NICE encourages further research into the use of innovative technologies for the management of severe acute respiratory failure, and may review this guidance on publication of further evidence. **Short-term circulatory support with left ventricular assist devices as a bridge to cardiac transplantation or recovery. NICE Interventional procedure guidance 177 (2006).** 1.1 Limited evidence on the safety and efficacy of short-term circulatory support with left ventricular assist devices (LVADs) as a bridge to cardiac transplantation or recovery appears adequate to support the use of this procedure provided that the normal arrangements are in place for audit and clinical governance. 1.2 Clinicians should ensure that patients fully understand the high complication rates associated with this procedure and that the procedure is a temporary measure. In addition, use of the Institute's information for the public is recommended. 1.3 Publication of further research will be useful, particularly on the use of this procedure in patients with cardiogenic shock following acute myocardial infarction.

	Extracorporeal membrane oxygenation (ECMO) in post neonatal children NICE Interventional procedure guidance 38 (2004). 1.1 Current evidence on the safety and efficacy of extracorporeal membrane oxygenation in postneonatal children appears adequate to support the use of this procedure, provided that the normal arrangements are in place for consent, audit and clinical governance. 1.2 All children undergoing this treatment, including those treated after cardiopulmonary bypass, should be entered onto the international registry of the Extracorporeal Life Support Organization (ELSO), based at the University of Michigan, USA.

Appendix C: Literature search for extracorporeal membrane oxygenation (ECMO) for acute heart failure in adults

Database	Date searched	Version/files
Cochrane Database of Systematic Reviews – CDSR (Cochrane Library)	26/03/2013	Issue 2 of 12, February 2013
Database of Abstracts of Reviews of Effects – DARE (CRD website)	26/03/2013	Issue 1 of 4, January 2013
HTA database (CRD website)	26/03/2013	Issue 1 of 4, January 2013
Cochrane Central Database of Controlled Trials – CENTRAL (Cochrane Library)	26/03/2013	Issue 2 of 12, February 2013
MEDLINE (Ovid)	26/03/2013	1946 to March Week 2 2013
MEDLINE In-Process (Ovid)	26/03/2013	March 25, 2013
EMBASE (Ovid)	26/03/2013	1974 to 2013 Week 12
CINAHL (NLH Search 2.0/EBSCOhost)	26/03/2013	1981 to present
BLIC (Dialog DataStar)	26/03/2013	n/a

Trial sources searched on

- Current Controlled Trials *meta*Register of Controlled Trials – *m*RCT
- Clinicaltrials.gov
- National Institute for Health Research Clinical Research Network Coordinating Centre (NIHR CRN CC) Portfolio Database

Websites searched

- National Institute for Health and Care Excellence (NICE)
- Food and Drug Administration (FDA) - MAUDE database
- French Health Authority (FHA)
- Australian Safety and Efficacy Register of New Interventional Procedures – Surgical (ASERNIP – S)
- Australia and New Zealand Horizon Scanning Network (ANZHSN)
- Conference search
- Evidence Updates (NHS Evidence)
- General internet search

MEDLINE search strategy

1	Heart Failure/
2	Acute Disease/
3	1 and 2
4	Cardiomyopathies/
5	Shock, Cardiogenic/
6	Myocardial Stunning/
7	Myocarditis/
8	((acute* or sever*) adj2 (heart* or cardiac* or myocardial or cardio* or ventric*) adj2 (failure or decompensation or insufficient* or dysfunct* or "stand still")).tw.
9	((postpartum* or post-partum* or peripartum* or peri-partum*) adj3 cardiomyopath*).tw.
10	(cardiogenic* adj3 shock*).tw.
11	((myocardial* adj3 (stunn* or hibernat*)) or ((stunn* or hibernat*) adj3 myocard*)).tw.
12	myocardit*.tw.
13	or/3-12
14	Extracorporeal Membrane Oxygenation/
15	Extracorporeal Circulation/
16	Oxygenators, Membrane/
17	ECMO.tw.
18	(Extracorpor* adj3 membran* adj3 Oxygenat*).tw.
19	(Extracorpor* adj3 Circulat*).tw.
20	(membrane* adj3 oxygenator*).tw.
21	(Biomedicus adj3 pump*).tw.
22	(Maquet* adj3 rotaflow*).tw.
23	(Jostra adj3 (pump* or rotaflow*)).tw.
24	(Levitronix adj3 (Centrimag* or pump* or system* or oxygen*)).tw.
25	(Medos adj3 (Hilite* or oxygen*)).tw.
26	or/14-25
27	13 and 26
28	animals/ not humans/
29	27 not 28
30	limit 29 to english language
31	limit 30 to ed=19900101-20130331