

Extracorporeal carbon dioxide removal for acute respiratory failure

Interventional procedures guidance

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Your responsibility

This guidance represents the view of NICE, arrived at after careful consideration of the evidence available. When exercising their judgement, healthcare professionals are expected to take this guidance fully into account. However, the guidance does not override the individual responsibility of healthcare professionals to make decisions appropriate to the circumstances of the individual patient, in consultation with the patient and/or guardian or carer.

Commissioners and/or providers have a responsibility to implement the guidance, in their local context, in light of their duties to have due regard to the need to eliminate unlawful discrimination, advance equality of opportunity, and foster good relations. Nothing in this guidance should be interpreted in a way that would be inconsistent with compliance with those duties.

Commissioners and providers have a responsibility to promote an environmentally sustainable health and care system and should assess and reduce the environmental impact of implementing NICE recommendations wherever possible.

This guidance replaces IPG428.

1 Recommendations

- 1.1 Current evidence on the safety of extracorporeal carbon dioxide removal (ECCO₂R) for acute respiratory failure shows several serious but well-recognised complications. Evidence on its efficacy is limited in quality and quantity. Therefore, this procedure should only be used with special arrangements for clinical governance, consent, and audit or research.
- 1.2 Clinicians wishing to do ECCO₂R should:
- Inform the clinical governance leads in their trusts.
 - Ensure that patients (if possible) and their families or carers understand the uncertainty about the procedure's efficacy and the risk of complications and provide them with clear written information. In addition, the use of NICE's [information for the public](#) is recommended.
 - Audit and review clinical outcomes of all patients having ECCO₂R (see section 1.4 and [section 7.1](#)).
- 1.3 Only patients with potentially reversible acute respiratory failure or those being considered for lung transplantation should be selected for this procedure. ECCO₂R should only be used by specialist intensive care teams trained in its use.
- 1.4 NICE encourages clinicians to enter patients into ongoing trials such as the [protective ventilation with veno-venous lung assist in respiratory failure \(REST\)](#) trial, and to collaborate in data collection initiatives such as the [Extracorporeal Life Support Organization](#) register. Data collected should include information on patient selection criteria, thresholds for intervention, the type of ECCO₂R technique being used and clinical outcomes. NICE may update the guidance on publication of further evidence.

2 Indications and current treatments

- 2.1 Acute respiratory failure is a life-threatening condition that results in abnormally low oxygen levels (hypoxia) or abnormally high carbon dioxide (CO₂) levels (hypercapnia) in the blood. A particularly severe type of acute respiratory failure is acute respiratory distress syndrome, which is a disease process resulting from several conditions including sepsis, pneumonia or chest trauma.
- 2.2 Mechanical ventilation is the conventional treatment for acute respiratory failure. However, in some patients, hypoxia or hypercapnia cannot be adequately corrected. This is a particular problem when ventilation settings are reduced to minimise the risk of ventilator-induced lung injury. Extracorporeal CO₂ removal (ECCO₂R) may reduce blood CO₂ levels, allowing the reduction in the ventilation settings to be maintained.

3 The procedure

- 3.1 The aim of extracorporeal carbon dioxide removal (ECCO₂R) is to reduce blood CO₂ levels in acute respiratory failure, independently of the lungs. It can be used in cases of acute respiratory failure when a reduction in ventilator settings is needed to minimise the risk of ventilator-induced lung injury, but when such reductions (for example, airway pressures and tidal volume) result in severe hypercapnia. By allowing a reduction in ventilator settings, ECCO₂R may help to improve the likelihood and speed of lung recovery. The technique may also increase blood oxygen levels.
- 3.2 There are 2 main types of ECCO₂R: venovenous (VV) and arteriovenous (AV). In both types, cannulae are connected to a low-resistance synthetic membrane device where exchange of CO₂ occurs. In VV-ECCO₂R, either a single-access double lumen catheter or a dual-access system using 2 venous catheters is inserted into a large vein or veins (typically the femoral or internal jugular veins) and connected to a venovenous circuit. Flow across the membrane is maintained using a pump. In AV-ECCO₂R, an artery and a vein are cannulated (typically the femoral artery and femoral vein). Arterial blood pressure drives blood continuously through the device and it is returned through the vein.
- 3.3 ECCO₂R can be done using either a true ECCO₂R system or a modified

extracorporeal membrane oxygenation system.

- 3.4 Patients may be treated with ECCO₂R support for several weeks, depending on clinical need.

4 Efficacy

This section describes efficacy outcomes from the published literature that the committee considered as part of the evidence about this procedure. For more detailed information on the evidence, see the [interventional procedure overview](#).

- 4.1 In a multicentre randomised controlled trial (RCT) of 79 patients treated by low ventilation (about 3 ml/kg) combined with arteriovenous (AV) extracorporeal carbon dioxide removal (ECCO₂R; n=40) or an acute respiratory distress syndrome network strategy without ECCO₂R (about 6 ml/kg; n=39), 18% (7/40) of patients in the AV-ECCO₂R group died in hospital compared with 15% (6/39) in the control group (the difference between the 2 groups was not statistically significant). In an RCT of 40 patients treated by low-frequency positive-pressure ventilation and venovenous (VV) ECCO₂R (n=21) or continuous positive-pressure ventilation alone (n=19), survival rate at 30 days was 33% (7/21) in the group treated by VV-ECCO₂R compared with 42% (8/19) in the control group (p=0.56). In a systematic review including the 2 RCTs listed above and 12 observational studies, mortality rates of patients treated by VV- or AV-ECCO₂R ranged from 27% to 75% (mean 55.5%, standard deviations 74.2 to 60.3). In an analysis of UK patients on the Extracorporeal Life Support Organization register, the survival to discharge rate was 45% (27/60). Of those discharged, 48% (13/27) were discharged to home, and 41% (9/22) of patients receiving AV-ECCO₂R and 47% (18/38) receiving VV-ECCO₂R were discharged alive (the difference between the groups was not statistically significant). In an analysis of the Regensburg extracorporeal membrane oxygenation register data comparing the efficacy of different systems used to deliver ECCO₂R, 32% (196/317) of patients overall were discharged from hospital (range across devices 60% to 78%).
- 4.2 Three case series of patients treated by AV-ECCO₂R reported a statistically significant reduction in the partial pressure of CO₂ in arterial blood (PaCO₂) within 24 hours of initiating ECCO₂R support, compared with baseline. In the first case series of 90 patients, PaCO₂ decreased from a median of 60 mmHg to

34 mmHg at 24 hours ($p < 0.05$). In the second case series of 159 patients, PaCO₂ decreased from 67 mmHg to 35 mmHg at 24 hours ($p = 0.001$). In the third case series of 51 patients, PaCO₂ decreased from 73 mmHg at baseline to 41 mmHg at 24 hours ($p < 0.01$).

- 4.3 In the case series of 90 patients, there was a statistically significant increase in partial pressure of oxygen (PaO₂) to fraction of inspired oxygen (FiO₂) ratio from 58 mmHg at baseline to 101 mmHg at 24 hours ($p < 0.05$). In the case series of 51 patients, there was a statistically significant increase in PaO₂/FiO₂ from 75 mmHg at baseline to 110 mmHg at 24 hours ($p < 0.05$).
- 4.4 In the case series of 90 patients, median minute ventilation (MV) statistically significantly decreased from 13.0 litres/min at baseline to 9.9 litres/min at 24 hours ($p < 0.05$). In the case series of 159 patients, mean MV decreased from 13.8 litres/min to 11.6 litres/min (p value not stated). In the case series of 51 patients, median MV statistically significantly decreased from 11.5 litres/min to 6.6 litres/min ($p < 0.01$).
- 4.5 In the case series of 90 patients, median respiratory frequency statistically significantly decreased from 27 breaths/min at baseline to 23 breaths/min at 24 hours ($p < 0.05$). In the case series of 159 patients, there was a decrease from 32 breaths/min at baseline to 29 breaths/min at 24 hours (p value not stated). In the case series of 51 patients, there was a decrease from 25 breaths/min to 21 breaths/min at 24 hours (p value not stated). In a multicentre retrospective matched comparison study of 42 patients treated by pumpless extracorporeal lung assist (PECLA; $n = 21$) or invasive mechanical ventilation ($n = 21$), there was a decrease from a median number of 28 breaths/min (interquartile range [IQR] 25–31) at baseline to a median number of 21 breaths/min (IQR 17–25) at 21–24 hours for the PECLA group (p value not stated).
- 4.6 The specialist advisers listed the following key efficacy outcomes: mortality, ventilator-free days, length of stay in intensive care, intubation avoidance and lowering of CO₂ in the blood.

5 Safety

This section describes safety outcomes from the published literature that the committee considered as part of the evidence about this procedure. For more detailed information on the

evidence, see the [interventional procedure overview](#).

- 5.1 An analysis of the Extracorporeal Life Support Organization (ELSO) register data (22 had arteriovenous extracorporeal carbon dioxide removal [AV-ECCO₂R] and 38 had venovenous [VV] ECCO₂R) reported that 32% (19/60) of patients had complications. Of these 19 patients, 11 had a single complication and 8 had 2 or more complications. In a multicentre randomised controlled trial (RCT) of 79 patients treated by low ventilation (about 3 ml/kg) combined with AV-ECCO₂R (n=40) or an acute respiratory distress syndrome (ARDS) network strategy without ECCO₂R (about 6 ml/kg; n=39), 8% (3/40) of patients had ECCO₂R-related adverse reactions. In a meta-analysis of 8 case series (n=225 patients treated by AV-ECCO₂R), the complication rate was 29%. In a case series of 90 patients treated by AV-ECCO₂R, serious complications were reported in 24% of patients (22/90).
- 5.2 Limb ischaemia was reported in 9% (21/225) of patients in the meta-analysis of 8 case series. ECCO₂R-related ischaemia was reported in 1 patient in the RCT of 79 patients treated by low ventilation combined with AV-ECCO₂R (n=40) or an acute respiratory distress syndrome network strategy without ECCO₂R (n=39). Lower limb ischaemia was reported in 8% (13/159) of patients in a case series of 159 patients treated by AV-ECCO₂R; in these patients, the arterial cannula was either exchanged with a smaller one or moved to the contralateral femoral artery.
- 5.3 Central nervous system haemorrhage was reported in 1 patient out of 60 in the analysis of UK cases in the ELSO register data. Intracerebral haemorrhage was reported in 1 patient in the case series of 90 patients. Intracranial haemorrhage was reported in 1 patient in each arm of an RCT of 40 patients treated by low frequency positive-pressure ventilation and VV-ECCO₂R (n=21) or continuous positive-pressure ventilation alone (n=19). In the same study, intrapulmonic haemorrhage was reported in 19% (4/21) of patients treated by ECCO₂R. It was also reported that ECCO₂R had to be stopped in 7 patients because of haemorrhage.
- 5.4 Bleeding at the site of cannulation was reported in 12% (7/60) of patients in the UK patients of the ELSO register, in 4% (8/225) of patients in the meta-analysis of 8 case series, and in 1 patient in the case series of 51 patients. Diffuse bleeding and shock during cannulation was reported in 1 patient in the case

series of 90 patients (no further details provided).

- 5.5 Haematoma/aneurysm at the cannulation site was reported in 1 patient in the case series of 90 patients. 'False' aneurysm was reported in 5% (2/40) of patients treated by ECCO₂R in the RCT of 79 patients treated by low ventilation combined with AV-ECCO₂R or ARDS Network strategy without ECCO₂R. Pseudo aneurysm of the femoral artery was reported in 1 patient treated by pumpless extracorporeal lung assist (PECLA) in a multicentre retrospective matched comparison study of 42 patients treated by PECLA (n=21) or invasive mechanical ventilation (n=21).
- 5.6 Venous thrombosis was reported in 5% (1/21) of patients in the ECCO₂R arm and in 11% (2/19) of patients in the control arm in the RCT of 40 patients. The meta-analysis of 8 case series reported arterial thrombus formation in 2% of patients (5/225), venous thrombus formation in 5% (11/225) and oxygenator thrombus formation in 3% (6/225). Thrombus formation was reported in 17% (27/159) of patients in the case series of 159 patients; the oxygenators were exchanged. In the same study, thrombosis of the entire system developed in 8 patients (4 were inadequately anticoagulated, 2 had heparin-induced thrombocytopenia type II and there were 2 device failures). ECCO₂R circuit clotting was reported in 19% (4/21) of patients treated by VV-ECCO₂R in the RCT of 40 patients.
- 5.7 Infection was reported in 8% (5/60) of patients in the analysis of UK patients on the ELSO register. Infection was reported in 1 patient in the meta-analysis of 8 case series (n=225).
- 5.8 Compartment syndrome needing fasciotomy was reported in 3% (4/159) of patients in the case series of 159 patients; 1 of these patients needed lower leg amputation. Compartment syndrome was reported in 4% (4/90) of patients in the case series of 90 patients. Compartment syndrome was reported in 1 patient in the case series of 51 patients; this was surgically treated.
- 5.9 Renal complications were reported in 10% (6/60) of patients in the analysis of UK patients on the ELSO register.
- 5.10 Cardiovascular complications were reported in 10% (6/60) of patients in the analysis of UK patients on the ELSO register. Cardiac dysrhythmia was reported

in 10% (2/21) of patients in the ECCO₂R group and in 11% (2/19) of patients in the control group in the RCT of 40 patients; cardiac tamponade occurred in 5% (1/21) in the ECCO₂R group and 0% (0/19) in the control group.

- 5.11 Haemolysis was reported in 1 patient in the case series of 90 patients.
- 5.12 Technical problems were reported in 21% (15/70) of patients in a case series of 70 patients treated by AV-ECCO₂R. Mechanical complications were reported on 7 occasions in the analysis of UK patients on the ELSO register: 1 oxygenator failure, 2 pump malfunctions, 1 oxygenator clot, 2 other clots and 1 cannula problem. Plasma leakage was reported in 4% (10/225) of patients in the meta-analysis of 8 case series.
- 5.13 In addition to safety outcomes reported in the literature, specialist advisers are asked about anecdotal adverse events (events which they have heard about) and about theoretical adverse events (events which they think might possibly occur, even if they have never done so). For this procedure, specialist advisers did not list any anecdotal adverse events. They considered that allergic reaction was a theoretical adverse event.

6 Committee comments

- 6.1 The committee noted that there are several ongoing studies using extracorporeal carbon dioxide removal (ECCO₂R) in patients with acute exacerbation of chronic obstructive pulmonary disease. It may also be used to support weaning from ventilation and as a bridge to lung transplantation.
- 6.2 The committee noted that the technology for this procedure is evolving.
- 6.3 The committee noted that, although complications reported in the studies were common, patients selected for treatment by ECCO₂R had severe and life-threatening disease.

7 Further information

- 7.1 This guidance requires that clinicians doing the procedure make special arrangements for audit. NICE has identified relevant audit criteria and has

developed an [audit tool](#) (which is for use at local discretion).

7.2 For related NICE guidance, see the [NICE website](#).

Information for patients

NICE has produced information on this procedure for patients and carers ([information for the public](#)). It explains the nature of the procedure and the guidance issued by NICE, and has been written with patient consent in mind.

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Endorsing organisation

This guidance has been endorsed by [Healthcare Improvement Scotland](#).

Accreditation

