

NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Interventional procedure consultation document

Extracorporeal carbon dioxide removal for acute respiratory failure

Extracorporeal carbon dioxide removal is used to treat respiratory failure (when the lungs do not work effectively) in critically ill patients. The aim is to remove excess carbon dioxide from the blood. The patient still needs oxygen by mechanical ventilation. Blood is taken from the circulation, out of the body ('extracorporeal'). It is then passed through a synthetic membrane, where carbon dioxide is removed, before the blood is returned to the body.

The National Institute for Health and Care Excellence (NICE) is examining extracorporeal carbon dioxide removal for acute respiratory failure and will publish guidance on its safety and efficacy to the NHS. NICE's interventional procedures advisory committee has considered the available evidence and the views of specialist advisers, who are consultants with knowledge of the procedure. The advisory committee has made draft recommendations about extracorporeal carbon dioxide removal for acute respiratory failure.

This document summarises the procedure and sets out the draft recommendations made by the advisory committee. It has been prepared for public consultation. The advisory committee particularly welcomes:

- comments on the draft recommendations
- the identification of factual inaccuracies
- additional relevant evidence, with bibliographic references where possible.

Note that this document is not NICE's formal guidance on this procedure. The recommendations are provisional and may change after consultation.

The process that NICE will follow after the consultation period ends is as follows.

- The advisory committee will meet again to consider the original evidence and its draft recommendations in the light of the comments received during consultation.

- The advisory committee will then prepare draft guidance which will be the basis for NICE's guidance on the use of the procedure in the NHS.

For further details, see the [Interventional Procedures Programme process guide](#), which is available from the NICE website.

Through its guidance NICE is committed to promoting race and disability equality, equality between men and women, and to eliminating all forms of discrimination. One of the ways we do this is by trying to involve as wide a range of people and interest groups as possible in the development of our interventional procedures guidance. In particular, we aim to encourage people and organisations from groups who might not normally comment on our guidance to do so.

In order to help us promote equality through our guidance, we should be grateful if you would consider the following question:

Are there any issues that require special attention in light of NICE's duties to have due regard to the need to eliminate unlawful discrimination, advance equality of opportunity, and foster good relations between people with a characteristic protected by the equalities legislation and others?

Please note that NICE reserves the right to summarise and edit comments received during consultations or not to publish them at all where in the reasonable opinion of NICE, the comments are voluminous, publication would be unlawful or publication would otherwise be inappropriate.

Closing date for comments: 29th April 2016

Target date for publication of guidance: July 2016

1 Draft 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.

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- 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 sections 1.4 and 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 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, despite the maximum mechanical ventilation that the lungs can tolerate, without causing ventilator-induced lung injury. Extracorporeal carbon dioxide removal (ECCO₂R) may reduce blood carbon dioxide levels, allowing a reduction in the ventilation settings. It may also be used to support weaning from ventilation and as a bridge to lung transplantation.

3 The procedure

3.1 The aim of extracorporeal carbon dioxide removal (ECCO₂R) is primarily to reduce blood carbon dioxide levels and allow a reduction in ventilation settings (such as airway pressures and tidal volume). This may minimise the risk of ventilator-induced lung injury and 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 and arteriovenous. In both types, cannulae are connected to a low-resistance synthetic membrane device where exchange of carbon dioxide occurs. In venovenous 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 arteriovenous 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. Cannulation of the femoral artery may be associated with leg ischaemia.

- 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 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 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 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 venovenous 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 significant reduction in the partial pressure of carbon dioxide 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 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 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) 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 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 decreased significantly 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 CO_2 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 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 arteriovenous (AV) extracorporeal carbon dioxide removal (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), the complication rate was 29%. In a case series of 90 patients, 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 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 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 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 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 in patients with chronic obstructive pulmonary disease.
- 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 extracorporeal carbon dioxide removal 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 is developing an audit tool (which is for use at local discretion). This tool will be available when the guidance is published.

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

7.3 This guidance is a review of Extracorporeal membrane carbon dioxide removal NICE interventional procedure guidance 428 (2012).

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