history of COPD is far from being determined.

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ECMO in adults for severe respiratory failure finally comes of age: just in time?

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The idea of employing cardiopulmonary bypass technology as a means of oxygenating (extracorporeal membrane oxygenation (ECMO)) or removing carbon dioxide ($ECCO_2R$) in patients with acute respiratory failure (ARF) was first assessed in randomised controlled trials in the 1970s and 1980s.[1 2] Poor rates of survival and major complications, particularly massive haemorrhage, led to most intensivists believing that ECMO was inappropriate in adults. A small number of centres worldwide—including that in Leicester, UK—continued to refine the use of ECMO in small numbers of adult patients whom it proved impossible to oxygenate by conventional means. Following the publication of their case series with improved results,[3] Peek and colleagues embarked upon a randomised controlled trial of conventional ventilation or ECMO in patients with severe ARF (CESAR), the results of which have just been reported.[4]

Patients (n=766) were screened for inclusion over a 5-year period and those with potentially reversible severe ARF (defined as a Murray score >3 or uncontrolled hypercapnia (pH <7.20); n=188) were entered in the trial. Many had multiorgan failure. The mean PaO_2/FIO_2 ratio at study entry was 10 kPa, with a positive end-expiratory pressure of 14 cm H_2O. Exclusion criteria included irreversible disease, the receipt of high-pressure high-inspired oxygen ventilation for >7 days and contraindications to anticoagulation. Patients were randomised to receive conventional treatment at the referring hospital or an approved tertiary centre where they received mechanical ventilation alone (which could include

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oscillation, inhaled nitric oxide and prone positioning) or transfer to Leicester where, in addition, ECMO could be provided. Encouragingly, 63% of those allocated to the ECMO centre survived without severe disability at 6 months compared with 47% of those receiving conventional support. Economic analysis estimated the cost per additional quality of life year at about £20 000. The study was analysed on an intention-to-treat basis; the improved outcome occurred despite five patients dying before or during transfer and only 75% of those transferred received ECMO.

The publication of this study represents an extraordinary achievement. It was conceived and led in an atmosphere of scepticism among the critical care community, driven partly by the markedly improved outcomes for patients with acute lung injury that emerged following the development of new ventilatory techniques.[5] Furthermore, moving such critically ill patients is complex and difficult, and the fact that so few succumbed as a consequence is a testimony to the skill and dedication of the investigators.

By contrast, the study had significant limitations about which the authors are open. First, differences in non-ECMO-related therapies received by the intervention group might have explained its better outcome. Thus, patients receiving ECMO were more likely to be given corticosteroids and artificial liver support, although neither therapy alone has been shown to improve mortality in patients either with severe acute respiratory distress syndrome (ARDS)[6 7] or liver failure.[8] Second, patients moved to Leicester were more likely to receive low-volume low-pressure mechanical ventilation, a strategy that has been shown to improve outcome[5] and minimise further pulmonary injury.[9] However, whether this was because ECMO facilitated that goal by partially supporting gas exchange is not known.

What does the study mean for respiratory physicians, aside from those who also practise critical care? First and foremost it has shown that ECMO can safely bridge patients with reversible severe ARF to recovery without the complications documented previously. However, selecting the most appropriate patients to receive ECMO should involve those with the diagnostic and prognostic skills to identify the underlying pathology, the natural history of disease and the most appropriate adjunctive therapies. Second, survivors often require prolonged inpatient and outpatient care that necessitates respiratory expertise. Thus, the current study and others[10 11] demonstrate that, at 6 months, spirometric measurements are about 75% predicted while patients have ongoing pulmonary symptoms and reduced exercise capacity.

Where are the lessons for healthcare planners? The study provides powerful support for the concept that centralised care should be provided for patients with severe ARF, probably in a limited number of centres with the necessary resources and expertise including ECMO. Such centres should be able to collect and move patients on ECMO, a model adopted in Scandinavia and Germany. The perceived risk of transfer is a barrier for many referring clinicians. However, because of the limitations of the study, the precise place of ECMO in hypoxaemic adults will remain controversial, if only in terms of the threshold for its application. Thus, some patients will arrive in the receiving centre and be found not to require or be unsuitable for ECMO (20% in the current study). Establishing precise thresholds for referral is therefore likely to prove difficult.

The advent of H1N1 infection has focused attention on young critically ill patients with severe ARF. Data from Australia and Canada suggest that those who require intensive care develop severe refractory hypoxaemia for which ECMO may prove to be highly effective. Evidence is now available to suggest that building capacity to provide such support is timely.

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