Selected Summaries

Severe acute respiratory distress syndrome: Does ECMO have a role?

Combes A, Hajage D, Capellier G, Demoule A, Lavoué S, Guervilly C, Da Silva D, Zafrani L, Tirot P, Veber B, Maury E, Levy B, Cohen Y, Richard C, Kalfon P, Bouadma L, Mehdaoui H, Beduneau G, Lebreton G, Brochard L, Ferguson Nd, Fan E, Slutsky AS, Brodie D, Mercat A; Eolia Trial Group, Reva, and Ecmonet. (Sorbonne Université Inserm Unité Mixte de Recherche [UMRS] 1166, Institute of Cardiometabolism and Nutrition, Service De Médecine Intensive-Réanimation, Institut De Cardiologie, Assistance Publique-Hôpitaux De Paris [APHP] Hôpital Pitié-Salpêtrière, Département de Biostatistiques, Santé Publique et Information Médicale, Centre de Pharmacoépidémiologie, APHP Hôpital Pitié-Salpêtrière, Sorbonne Université, Unité de Recherche Clinique Pitié-Salpêtrière, Sorbonne Université Inserm UMRS 1158, Service de Médecine Intensive-Réanimation et Pneumologie, APHP Hôpital Pitié-Salpêtrière, Service de Médecine Intensive et Réanimation, Centre Hospitalier Universitaire [CHU] Saint Louis, Service de Médecine Intensive et Réanimation, CHU Saint Antoine, Service de Médecine Intensive et Réanimation, APHP Bichat Hospital, Diderot University, and Service de Chirurgie Thoracique et Cardiovasculaire, APHP Hôpital Pitié-Salpêtrière, Institut de Cardiologie, Paris, Service de Médecine Intensive et Réanimation, Besançon University Hospital, and Research Unit Equipe Avenir 3920 and Structure Fédérative de Recherche 4234, University of Franche Comté, Besançon, Service de Médecine Intensive et Réanimation, CHU Pontchaillou, Rennes, Service de Médecine Intensive et Réanimation, CHU Hôpital Nord, APHM, Marseille, Service de Médecine Intensive et Réanimation, CHU Saint Denis, Saint Denis, Service de Médecine Intensive et Réanimation, CHU Le Mans, Le Mans, Département D'anesthésie et Réanimation, CHU de Rouen, Service de Médecine Intensive et Réanimation, Rouen University Hospital, and Normandie University, Université de Rouen, Equipe Avenir 3830, Rouen University Hospital, Rouen, Service de Médecine Intensive et Réanimation, CHU Nancy and Inserm Unité 1116, Université de Lorraine, Nancy, Service de Médecine Intensive et Réanimation, CHU Avicenne, Bobigny, Service de Médecine Intensive et Réanimation, CHU Kremlin Bicêtre, Le Kremlin Bicêtre, Service de Réanimation Polyvalente, Hôpital de Chartres, Chartres, CHU Martinique, Fort-De-France, and Service de Médecine Intensive et Réanimation, Centre Hospitalier Universitaire D'angers, Université D'angers, Angers, all in France; the Interdepartmental Division of Critical Care Medicine, Departments of Medicine and Physiology, Institute for Health Management, Policy, and Evaluation, University of Toronto, Keenan Research Center, Li Ka Shing Knowledge Institute, St Michael's Hospital, and The Department of Medicine, Division of Respirology, University Health Network and Sinai Health System, Toronto General Hospital, Toronto, Canada; and The Division of Pulmonary, Allergy, and Critical Care Medicine, Columbia University Medical Center, and New York-Presbyterian Hospital, Columbia University, New York, USA.) Extracorporeal membrane oxygenation for severe acute respiratory distress syndrome. *N Engl J Med* 2018;**378:**1965–75.

SUMMARY

In this international multicentre study the authors compared the efficacy of veno-venous extracorporeal membrane oxygenation (ECMO) as the primary treatment modality in patients with severe acute respiratory distress syndrome (ARDS) with standardized conventional ventilatory management in the control group, with the possibility of a crossover from the ventilator (control) group to the ECMO group if conventional management failed, resulting in refractory respiratory failure and decompensated haemodynamics not responding to inotropic support.

A total of 124 patients were randomized to the ECMO group of which 44 patients (35%) had died at 60 days whereas in the control group receiving conventional ventilation 57 of 125 patients (46%) died (p=0.09). Hence, there was no statistically significant outcome difference between the 2 treatment methods used for patients with ARDS regarding 60-day mortality. However, a crossover from the control group to the ECMO group was required in 35 patients (28%) of the control group, who had worsened with conventional ventilatory management and 20 of these 35 patients (57%) died despite ECMO support, because these patients were naturally much sicker at the time of crossover to the ECMO group as compared to the patients who had been primarily randomized to the ECMO group at the beginning of the study (35% mortality). There was a slightly increased risk of bleeding requiring transfusion in the ECMO group 46% versus 28%, and a higher incidence of severe thrombocytopenia—27% in the ECMO versus 16% in the control group. However, there was a lower incidence of ischaemic stroke in the ECMO (0) than that in the control group (5%). The authors concluded that in patients with severe ARDS, 60-day mortality was not lower with use of ECMO as compared to a strategy using conventional mechanical ventilation.

COMMENT

The first author of this article, Alain Combes from France, is a highly respected professional in the field of ECMO. The results of this trial, also called the EOLIA trial (ECMO to rescue lung injury in severe ARDS), were awaited for a long time. The trial enrolled 249 patients from various countries over a period of 6 years and its outcome was eagerly awaited.

The only available earlier, major randomized multicentre trial comparing ECMO and conventional ventilation for ARDS in adults was the CESAR trial (conventional ventilator support versus extracorporeal membrane oxygenation for severe adult respiratory failure).[1] This trial was a large multicentre trial done in the UK, but was not as well designed because of the use of a variety of non-standardized ventilatory strategies in the control group, and a large number of patients in the ECMO group who were transferred to designated advanced ECMO centres but did not receive ECMO support at all, and instead were given ventilatory therapy on the basis of clinical assessment at advanced centres.

All these deficiencies were removed from the trial design of the EOLIA trial. Here, all patients in the control group received a standardized 'lung protective' ventilation strategy with low tidal volumes, high respiratory rates, standardized positive end-expiratory pressure, FiO_2 and plateau pressures, use of prone positioning in 95% of patients and use of inhaled nitric oxide in a large number of patients. Conservative fluid management was used in all patients in the control group. ECMO support was

provided to all patients randomized to the ECMO group at centres experienced in providing ECMO support.

The results of the EOLIA trial are, however, tempered by the fact that the trial was stopped before recruitment was completed (only 75% sample size achieved) because the futility threshold of treatment was reached, i.e. the results showed that the treatment offered (ECMO) was not superior to conventional treatment. The Data and Safety Monitoring Board which was overlooking this trial stopped subsequent enrolment of patients because it wanted to protect new patients from continued randomization to the ECMO group whose results were not statistically superior to the control group.[2] Another noteworthy fact that complicates interpretation of the results is that 35 of 124 (28%) patients from the control group were transferred to the ECMO group when ventilatory management failed and 20 of these patients (57%) died despite ECMO support. Had these crossover patients continued in the control group all of them may have died, thereby affecting the final results in the control group.

The controversy surrounding the continued use of veno-venous ECMO for ARDS will persist despite the results of this much awaited EOLIA trial. However, the use of ECMO in several new situations is increasing day by day, including the use of veno-arterial ECMO for cardiorespiratory depression from various causes such as poisoning including organophosphorous poisoning, various chemical poisons, after snake bite, in severe sepsis, as a part of extracorporeal cardiopulmonary resuscitation (ECMO-assisted cardiopulmonary resuscitation), after myocardial depression from chemotherapy for cancers, in stabilization of brain dead donors for organ harvest, after viral myocarditis, in the catheterization laboratory for sick patients, such as ECMO supported percutaneous intervention for patients in cardiogenic shock. It is also being used for percutaneous transcatheter aortic valve replacement using ECMO support in patients considered too sick for conventional cardiac surgery. Catheter ablation of ventricular tachycardia using ECMO support for haemodynamic instability is another important use for veno-arterial ECMO. Pregnant patients with cardiac disease resulting in acute cardiac decompensation is another area where veno-arterial ECMO is life-saving for the conduct of safer labour, delivery or caesarean section, especially in parturients who develop peripartum cardiomyopathy. Non-cardiac surgery where ECMO has been found useful includes patients undergoing lung transplantation or thoracic and airway surgery, and large mediastinal or cervical masses which can compromise the airway after anaesthetic induction. Severe chest trauma could result in several complications such as tension pneumothorax, cardiac tamponade, haemorrhagic pericardial effusion injury to the heart, lungs, major blood vessels. These compromised patients would benefit from the use of ECMO.[3]

Despite the non-conclusive results from the EOLIA trial, the use of ECMO will continue for patients with severe ARDS, although not as the primary mode of treatment but only when failure of ventilatory management obligates its use.

Conflicts of interest. None declared

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