# Blood Conservation in Extracorporeal Membrane Oxygenation for Acute Respiratory Distress Syndrome

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*Background.* **Extracorporeal membrane oxygenation support (ECMO) typically requires multiple blood transfusions and is associated with frequent bleeding complications. Blood transfusions are known to increase morbidity and mortality in critically ill patients, which may extend to patients receiving ECMO. Aiming to reduce transfusion requirements, we implemented a blood conservation protocol in adults with severe acute respiratory distress syndrome (ARDS) receiving ECMO.**

*Methods.* **This was a retrospective study of adults receiving ECMO for ARDS after initiation of a blood conservation protocol that included a transfusion trigger of hemoglobin of less than 7.0 g/dL, use of low-dose anticoagulation targeting an activated partial thromboplastin time of 40 to 60 seconds, and autotransfusion of circuit blood during decannulation. The primary objective was to evaluate transfusion requirements during ECMO support. Clinical outcomes included survival, neurologic function, renal function, bleeding, and thrombotic complications.**

*Results.* **The analysis included 38 patients; of these, 24 (63.2%) received a transfusion while receiving ECMO. Median hemoglobin was 8.29 g/dL. A median of 1.0 units (range, 250 to 300 mL) was transfused during ECMO support over a median duration of 9.0 days, equivalent to 0.11 U/d (range, 27.5 to 33.3 mL/d). The median activated partial thromboplastin time was 46.5 seconds. Bleeding occurred in 10 patients (26.3%); severe bleeding occurred in 2 patients (5.3%). Twenty-eight patients (73.7%) survived to hospital discharge.**

*Conclusions.* **Implementation of a blood conservation protocol in adults receiving ECMO for ARDS resulted in lower transfusion requirements and bleeding complications than previously reported in the literature and was associated with comparable survival and organ recovery.**

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Advances in extracorporeal membrane oxygenation (ECMO) technology have made it safer and easier to use [1]. Interest in ECMO surged during the 2009 influenza A (H1N1) pandemic in adult patients with severe acute respiratory distress syndrome (ARDS) [2] and after the publication of a randomized controlled trial of ECMO for adults with acute respiratory failure [3]. The optimal medical management of patients receiving ECMO, including the transfusion threshold and the degree of anticoagulation, has not been established, however.

The Extracorporeal Life Support Organization recommends that patients receive a transfusion to a normal hemoglobin of 12 to 14 g/dL [4], which frequently requires transfusion of 2 to 3 units of packed red blood cells (pRBCs) daily [5–9], although requirements of up to 6 U/d have been reported [10]. Many ECMO centers follow this approach, although the optimal transfusion threshold remains a source of controversy. Compared with conservative approaches to blood transfusion that accept a moderate degree of anemia and a hemoglobin as low as 7.0 g/dL, liberal strategies that transfuse to normal or nearly normal hemoglobin levels increase morbidity and mortality in critically ill patients [11–14]; this may extend to patients receiving ECMO. Traditional management of ECMO patients also includes high levels of anticoagulation [4] and is associated with frequent bleeding complications [2, 4].

To reduce transfusions, we implemented a three-part blood conservation protocol for patients receiving ECMO for ARDS that included use of a restrictive transfusion strategy [12]. We accept a hemoglobin level as low as 7.0 g/dL, use low-dose anticoagulation, and autotransfuse the blood within the circuit at the time of ECMO decannulation, thereby preserving RBC mass and minimizing blood loss to the circuit. We examined

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**Abbreviations and Acronyms**

APACHE II = Acute Physiology and Chronic Health Evaluation II
aPTT = activated partial thromboplastin time
ARDS = acute respiratory distress syndrome
ECMO = extracorporeal membrane oxygenation
$F_{DO_2}$ = fraction of delivered oxygen
$F_{IO_2}$ = fraction of inspired oxygen
GFR = glomerular filtration rate
IQR = interquartile range
$Pa_{O_2}$ = partial pressure of arterial oxygen
PEEP = positive end-expiratory pressure
pRBCs = packed red blood cells

our transfusion requirements, bleeding complications, and clinical outcomes after the implementation of this approach.

## Material and Methods

This study, which was approved by the Columbia University Investigational Review Board and performed in accordance with accepted ethical standards, included adults who received ECMO for ARDS in the medical intensive care unit at New York-Presbyterian Hospital/Columbia University College of Physicians and Surgeons between January 1, 2010, and December 31, 2012, the initial 3-year period after the formal adoption of our blood conservation protocol. We hypothesized that this approach would result in fewer pRBC transfusions and bleeding complications than previously reported. The primary objective was to quantify the units of pRBCs transfused during ECMO support. Secondary objectives were to characterize bleeding and thrombotic complications, survival to intensive care unit and hospital discharge, and neurologic and renal function after recovery.

ARDS was defined according to the Berlin criteria [15]. The decision to initiate ECMO support was at the discretion of our center's ECMO team, which included a pulmonary intensivist and thoracic surgeon. Patients considered for ECMO met criteria for severe ARDS with any of the following: a partial pressure of arterial oxygen–to–fraction of inspired oxygen ratio of less than 80 mm Hg, uncompensated hypercapnia with a pH of less than 7.15, or excessively high plateau pressures exceeding 35 to 45 cm $H_2O$, despite optimized ventilator management [1].

Most patients were cannulated by our center's mobile ECMO transport team and transferred to our institution on ECMO; therefore, use of other rescue therapies varied by availability at the patient's originating hospital. Relative contraindications to ECMO included advanced age, prolonged high-pressure ventilation, or any condition limiting the likelihood of benefit from ECMO, such as irreversible neurologic injury or metastatic cancer [1]. Shock, renal failure, acute liver injury, known bleeding diatheses, trauma (including traumatic brain injury), or refusal to accept blood products were not considered contraindications to ECMO.

Patients were managed with a three-part blood conservation protocol that included a RBC transfusion trigger of hemoglobin of less than 7.0 g/dL, an activated partial thromboplastin time (aPTT) goal between 40 and 60 seconds, and autotransfusion of circuit blood during decannulation. Anticoagulation was administered by continuous infusion and titrated according to a clinician-driven protocol. Patients diagnosed with a deep venous thrombosis were managed with therapeutic levels of intravenous anticoagulation. Aspirin was not routinely used. Although not a formal component of our protocol, our center takes a parsimonious approach to phlebotomy. The frequency of laboratory monitoring is at the clinician's discretion and occurs at least daily; gases are not routinely measured before and after oxygenator initiation.

Throughout the study period, ECMO circuit components included a centrifugal pump, polymethylpentene oxygenator, heat exchanger, and monitors of pressure before and after oxygenator initiation. Demographic, clinical, and laboratory data were obtained from our institution's electronic medical record. The median hemoglobin was obtained during the period the patient received ECMO. Transfusion requirements were measured as the number of units and milliliters of pRBCs transfused. At our institution, each unit of blood contains 250 to 300 mL of pRBCs.

Data are presented as median values with interquartile range (IQR). The glomerular filtration rate (GFR) was calculated using the Modification of Diet in Renal Disease Equation [16]. Normal GFR was reported as exceeding 60 mL/min/1.73 $m^2$ [17]. Data were analyzed with SAS 9.2 software (SAS Institute Inc, Cary, NC) and Excel 14.2.2 software (Microsoft Corp, Redmond, WA).

## Results

During the study period, 38 patients received ECMO for ARDS. Demographic data and pre-ECMO characteristics are listed in Table 1. Initial ECMO support was venovenous in 34 patients (89.4%), venoarterial in 2 (5.3%), and venoarterial venous in 2 (5.3%; Table 2). Median ECMO blood flow before weaning was 4.1 L/min (IQR, 3.8 to 4.7 L/min). The median ratio of ECMO blood flow to predicted cardiac output was 0.87 (IQR, 0.8 to 1). Median sweep gas flow was 3.4 L/min (IQR, 2.3 to 5.2 L/min), fraction of delivered oxygen was 1.0, and the preoxygenator saturation was 74.5% (IQR, 68.1% to 81%). The median duration of ECMO support was 9 days (IQR, 7 to 11.5 days).

The median hemoglobin during ECMO support was 8.2 g/dL (IQR 7.9 to 8.7 g/dL), with values of 9.1 g/dL at cannulation and 8.1 g/dL at decannulation (Table 3). At the time of cannulation, the study population had a platelet count of 163,000/mL (IQR 128,500 to 219,000/mL), a prothrombin time of 17.5 seconds (IQR, 15.8 to 18.4 seconds), international normalized ratio of 1.4 (IQR, 1.2 to 1.5),