Critical Care

RESEARCH LETTER

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Evaluation of right ventricular function and driving pressure with blood gas analysis could better select patients eligible for VV ECMO in severe ARDS

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To the Editor,

The Acute Respiratory Distress Syndrome (ARDS) is still associated with high mortality [1], despite application of recent guidelines [2, 3]. The EOLIA study suggested that Extra- Corporeal Membrane Oxygenation (ECMO) could be effective in some of the most severe patients, but failed to demonstrate a 20% increase in survival [4]. One reason could be that criteria for selecting patients were only based on blood gas analysis. Our hypothesis is that adding other factors could allow a better selection of patients who could benefit from ECMO.

We took advantages to have a large multicentric cohort of patients under protective ventilation for moderate-to-severe ARDS [5] to determine the incidence, characteristics and outcome of patients eligible for ECMO according to EOLIA-based criteria and to identify patients who would benefit the most of the technique. ECMO was only used in these centers as a recue therapy.

Mechanical ventilation was applied in the volume-assist control mode, with a target tidal volume (TV) of 6–8 mL/kg (predicted body weight) and a plateau pressure < 30 cmH_2O. Respiratory rate could be increased in case of high arterial carbon dioxide partial pressure ($PaCO_2$). Prone positioning was left to the discretion of the attending physician, but was typically performed in patients with a $PaO_2/FiO_2 < 100$ mmHg and/or an acute core pulmonale (ACP) [6]. Patients eligible for ECMO according to EOLIA-based criteria were identified as follows: $PaO_2/FiO_2 < 80$ mmHg with optimal PEEP, or a pH < 7.25 and $PaCO_2 > 60$ mmHg with a respiratory rate ≥ 35 cycles/min, despite the use of prone positioning or nitric oxide inhalation.

Statistical analysis was performed with R.4.0.4. Patients eligible for ECMO were compared to the rest of the cohort. Continuous data, expressed as medians (interquartile ranges), were compared with Mann–Whitney test. Categorical variables, expressed as numbers and percentages, were compared using the chi-square test or Fisher exact test. To evaluate independent factors associated with ICU mortality in this identified subgroup of patients, significant or marginally significant ($p < 0.10$) bivariate risk factors were examined using univariate and multivariable backward stepwise mixed logistic regression stratified on the center. SAPS II was forced in the model.

752 patients were studied. Characteristics and outcome are given in the Table 1. 67 (9%) patients were potentially eligible for ECMO. They had lower PaO_2/FiO_2 (62 [55–72] versus 114 [90–120] mmHg: $p < 0.01$) and higher incidence of ACP (42% versus 20%, $p < 0.001$). Only 8 of them underwent the procedure.

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Table 1 Clinical characteristics and outcome of the entire cohort according to EOLIA criteria

Characteristics, outcomes and complications	ARDS patients without EOLIA criteria (*n* = 685)	ARDS patients with EOLIA criteria (*n* = 67)	*p*-value
Age (years)	59 (47–72)	56 (47–70)	0.43
Male sex, *n* (%)	465 (68)	42 (63)	0.47
SAPS II	51 (38–65)	47 (33–64)	0.27
Weight (kg)	77 (65–84)	70 (59–86)	0.43
Cause of ARDS, *n* (%)			0.20
Pneumonia	83 (12)	8 (12)	
Aspiration	259 (39)	34 (51))	
Non-pulmonary sepsis	245 (37)	17 (26)	
Other causes	83 (12)	7 (11)	
Respiratory setting at inclusion			
Tidal volume (ml/kg)	6.7 (6.0–8.0)	6.02 (5.4–6.9)	< 0.01
Respiratory rate (cycle/min)	22 (16–27)	26 (22–30)	< 0.01
PEEP (cmH_2O)	8 (5–10)	10 (7–12)	< 0.01
Plateau pressure (cmH_2O)	24 (21–28)	27 (25–29)	< 0.01
Compliance (ml/cmH_2O)	30.7 (24–39.1)	25.9 (19.3–33.8)	< 0.01
Driving pressure (cmH_2O)	15 (13–19)	17 (14–19.8)	0.04
Arterial blood gases			
PaO_2/FiO_2 ratio (mmHg)	114 (90–120)	62 (55–72)	< 0.01
$PaCO_2$ (mmHg)	44 (38–52)	48 (41–60)	< 0.01
Shock, *n* (%)	449 (66)	53 (79)	0.04
Prone positioning, *n* (%)	163 (24)	55 (82)	< 0.01
VV ECMO in rescue during ARDS course, *n* (%)	0 (0)	8 (12)	< 0.01
RRT during ARDS course, *n* (%)	126 (30)	15 (40)	0.27
Echocardiographic findings			
RVEDA/LVEDA	0.68 (0.57–0.81)	0.83 (0.64–1.04)	< 0.01
Systolic pulmonary artery pressure (mmHg)	35 (20–48)	52 (35–59)	< 0.01
Severe acute cor pulmonale	43 (6)	11 (16)	< 0.01
Outcome, *n* (%)			
ICU mortality	243 (36)	31 (46)	0.10
ICU stay (days)	16 (8–30)	15 (6–31)	0.43

Values are expressed as median (interquartile range) or *n* (%)

ARDS, Acute Respiratory Distress Syndrome; PEEP, Positive End-Expiratory Pressure; VV ECMO, Veno-Venous Extracorporeal Membrane Oxygenation; RRT, Renal Remplacement Therapy; RVEDA, Right Ventricular End-Diastolic Area; LVDEA, Left Ventricular End-Diastolic Area; ICU, Intensive Care Unit

In-ICU mortality in the whole cohort was 36%. Causes of death in patients eligible for ECMO was multi-organ failure in 21 (68%), neurologic in 4 (13%) and ECMO complication in 3 (10%). Only 3 patients (10%) died from hypoxic cardiac arrest.

Characteristics and outcome of patients potentially eligible for ECMO according to ICU mortality are given in the Table 2. In multivariable analysis, severe right ventricular dilatation (right-to-left ventricle end-diastolic area ratio > 1) and driving pressure were the only factors associated with in-ICU mortality (OR [95% CI]: 5.62 [1.44–27.39], $p = 0.02$ and 1.14 [1.01–1.31], $p = 0.04$, respectively).

A limitation of our study is that eight patients of the cohort received ECMO as a rescue therapy, which may have influenced our results, especially since the technique is now safer when performed in expert centers. However, six of these eight patients died.

In conclusion, we report a 9% incidence of patients who reach the EOLIA-based criteria for ECMO in a large non-selected cohort of ARDS patients ventilated with moderate-to-severe ARDS. These patients exhibited higher driving pressure and more frequent right ventricle failure, both being independently associated with ICU mortality. How this subgroup of patients could be considered as the ideal target for ECMO

Table 2 Clinical characteristics and echocardiographic findings of ARDS patients eligible for ECMO

Characteristics, outcomes and complications	Survivors ($n=36$)	Non survivors ($n=31$)	*p*-value
Age (years)	56 (45–70)	57 (48–70)	0.44
Male sex, *n* (%)	23 (64)	19 (61)	0.47
SAPS II	44 (32–58)	53 (36–75)	0.15
Weight (kg)	74 (63–97)	67 (56–80)	0.22
Cause of ARDS, *n* (%)			0.63
Pneumonia	6 (17)	2 (7)	
Aspiration	18 (50))	16 (53)	
Non-pulmonary sepsis	8 (22)	9 (30)	
Other causes	4 (11)	3 (10)	
Respiratory setting at inclusion			
Tidal volume (ml/kg)	6.3 (5.5–7.6)	5.9 (5.3–6.6)	0.13
Respiratory rate (cycle/min)	25 (20–27)	30 (25–30)	< 0.01
PEEP (cmH_2O)	10 (8–12)	10 (7–12)	0.72
Plateau pressure (cmH_2O)	26 (24–29)	28 (25–38)	0.07
Compliance (ml/cmH_2O)	30 (2338)	23 (16–28)	< 0.01
Driving pressure (cmH_2O)	16 (14–19)	19 (16–22)	0.05
Arterial blood gases			
PaO_2/FiO_2 ratio (mmHg)	69 (58–74)	60 (55–67)	0.08
$PaCO_2$ (mmHg)	48 (40–52)	51 (42–70)	0.17
Shock, *n* (%)	25 (70)	28 (90)	0.07
Prone positioning, *n* (%)	31 (86)	24 (77)	0.52
VV ECMO in rescue during ARDS course, *n* (%)	2 (1)	6 (19)	0.13
RRT during ARDS course, *n* (%)	9 (33)	6 (55)	0.28
Echocardiographic findings			
RVEDA/LVEDA	0.71 (0.57–0.93)	0.98 (0.71–1.10)	0.10
Pulmonary hypertension (mmHg)	51 (44–55)	52 (34–63)	0.85
Severe acute cor pulmonale	3 (8)	8 (26)	0.09
ICU stay (days)	19 (14–34)	12 (3–20)	0.16

Values are expressed as median (interquartile range) or *n* (%)

ARDS, Acute Respiratory Distress Syndrome; PEEP, Positive End-Expiratory Pressure; VV ECMO, Veno-Venous Extracorporeal Membrane Oxygenation; RRT, Renal Remplacement Therapy; RVEDA, Right Ventricular End-Diastolic Area; LVDEA, Left Ventricular End-Diastolic Area; ICU, Intensive Care Unit

selection strategy should better be evaluated in the future.

Abbreviations

ARDS: Acute Respiratory Distress Syndrome; ECMO: Extra-Corporeal Membrane Oxygenation; TV: Tidal Volume; ACP: Acute Core Pulmonale; PEEP: Positive End Expiratory Pressure; SAPS II: Simplified Acute Physiology Score II; ICU: Intensive Care Unit; RRT: Renal Replacement Therapy; RVEDA: Right Ventricular End-Diastolic Area; LVDEA: Left Ventricular End-Diastolic Area.

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Authors' contributions

MP and AVB designed the study; AMD, PV, PM, AL collected the data, MP did the statistical analysis, MP and AVB wrote the manuscript; all authors reviewed the manuscript. All authors read and approved the final manuscript.

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Availability of data and materials

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Declaration

Ethics approval and consent to participate

The study was approved by the Institutional Review Boards of participating centers as a component of standard of care and requirement for patient's consent was waived.

Consent for publication

Not applicable.

Competing interests

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