Validation of RESP and PRESERVE score for ARDS patients with pumpless Extracorporeal Lung Assist (pECLA)

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Abstract

Background: RESP score and PRESERVE score have been validated for veno-venous Extracorporeal Membrane Oxygenation in severe ARDS to assume individual mortality risk. ARDS patients with low-flow Extracorporeal Carbon Dioxide Removal, especially pumpless Extracorporeal Lung Assist, have also a high mortality rate, but there are no validated specific or general outcome scores.

Methods: In a retrospective single center cohort study we calculated and evaluated RESP, PRESERVE, and SOFA score for 73 ARDS patients with pumpless Extracorporeal Lung Assist. Additionally, demographic data and hospital mortality as well as ventilator settings, hemodynamic parameters, and blood gas measurement before and during extracorporeal therapy were recorded.

Results: Pumpless Extracorporeal Lung Assist of mechanical ventilated ARDS patients resulted in an optimized lung protective ventilation, significant reduction of PaCO2, and compensation of acidosis. Scoring showed a mean score of alive versus deceased patients of 3 ± 1 versus -1 ± 1 for RESP ($p < 0.01$), 3 ± 0 versus 6 ± 0 for PRESERVE ($p < 0.05$) and 8 ± 1 versus 10 ± 1 for SOFA ($p < 0.05$). Using receiver operating characteristic curves, area under the curve (AUC) was 0.78 (95 % confidence interval (CI) 0.67 – 0.89, $p < 0.01$) for RESP score, 0.80 (95 % CI 0.70 – 0.90, $p < 0.0001$) for PRESERVE score and 0.66 (95 % CI 0.53 – 0.79, $p < 0.05$) for SOFA score.

Conclusions: RESP and PRESERVE scores were superior to SOFA, as non-specific critical care score. Although scores were developed for veno-venous ECMO, we could validate RESP and PRESERVE score for pumpless Extracorporeal Lung Assist. In conclusion, RESP and PRESERVE score are suitable to estimate mortality risk of ARDS patients with an arterio-venous pumpless Extracorporeal Carbon Dioxide Removal.

Background

Specific mortality risk scores, especially the Respiratory ECMO Survival Prediction (RESP) score (1) and the PRedicting dEath for SEvere ARDS on VV-ECMO (PRESERVE) score (2), were developed and validated for ARDS patients with veno-venous high-flow Extracorporeal Membrane Oxygenation (ECMO). ARDS with severe hypercapnia without life-threatening hypoxemia can be treated with Extracorporeal Carbon Dioxide Removal ($ECCO_2R$), especially pumpless Extracorporeal Lung Assist (pECLA). Despite a high mortality rate validated risk scores are lacking for these devices.

During the past decade, ECMO was frequently used for patients suffering severe hypoxemic ARDS. The experiences of H1N1 pandemic in 2009 (3, 4) and following clinical trials (5) reinforced the effort of establishing Extracorporeal Membrane Oxygenation as a salvage therapy. Extracorporeal oxygenation and decarboxylation maintains gas exchange and facilitates lung protective ventilation in severe ARDS (6). However, ECMO therapy remains a dangerous and invasive technology with a high rate of complications such as bleeding, infection, and mechanical complications (5–7).

In ARDS patients with severe hypercapnia and respiratory acidosis without life-threatening hypoxemia $ECCO_2R$ was propagated to achieve lung protective ventilation (8). Arterio-venous pECLA represents a specific subgroup of $ECCO_2R$ using a simplified extracorporeal lung assist technique for patients with hypercapnia and respiratory acidosis without cardiac failure. It demonstrated efficient extracorporeal carbon dioxide elimination resulting in lung protective ventilation without respiratory acidosis (9). Compared to veno-venous ECMO, pECLA requires less anticoagulation and the absence of a pump induces less mechanical stress to the blood. Furthermore, the simplified extracorporeal system bears lower risk of technical complications and shortened equipment. However, the pumpless extracorporeal lung assist requires a sufficient cardiac output as driving force for the pECLA and a femoral arterial cannulation bearing the risk of consecutive limb ischemia (10). Another limitation of pECLA therapy is an only moderate increase of oxygenation, although the combination of extracorporeal decarboxylation and lung protective ventilation reduces the risk of ventilator induced lung injury (VILI) (9, 11, 12).

High mortality rates of ECMO and allocation of limited ECMO resources were leading to the development of mortality prediction scores for veno-venous ECMO in severe ARDS. Especially the RESP score (1) and the PRESERVE score (2) have been used to identify risk factors for death of ECMO patients (additional file 1 and 2). Additionally, non-ARDS-specific scores have been used in critical care. The Sequential Organ Failure Assessment (SOFA) score, published in 1996, evaluates morbidity by scoring the organ failure of lung, coagulation, liver, cardiovascular system, brain, and kidney (additional file 3) (13). In the prospective observational LUNG SAFE study SOFA score was associated with outcome of ARDS (14).

RESP and/or PRESERVE scores have been compared and evaluated in several studies for ECMO therapy (15–21), but both scores as well as SOFA score have not been validated for ARDS patients treated with a primary extracorporeal CO_2 removal, like pECLA. Goal of our retrospective study was the evaluation of RESP and PRESERVE score to assume mortality risk of pECLA therapy in case of ARDS compared to SOFA score (1, 2, 13).

Methods

We conducted a retrospective single center cohort study of ARDS patients undergoing pECLA therapy between 2002 and 2016 at RWTH Aachen University Hospital to validate RESP, PRESERVE and SOFA score. General ethical approval was received by the RWTH Aachen University regional research ethics committee for retrospective studies (AF 047/16). Inclusion criteria were ARDS according to the Berlin criteria (22) with pECLA therapy and exclusion criteria missing data necessary for calculation of scores.

Standard therapy included a lung protective ventilation strategy with a pressure controlled ventilation mode, usually Biphasic Positive Airway Pressure ventilation: Additionally prone position was initiated in moderate to severe ARDS and inhaled nitric oxide was used as rescue therapy in hypoxemia according to the local standard. In our institution, indication for pECLA and ECMO is confirmed multidisciplinary by physicians of all involved medical faculties. In case of severe hypoxemia due to ARDS, patients were treated with veno-venous ECMO as rescue therapy. Severe hypercapnia especially in case of concomitant respiratory acidosis as well as achievement of lung protective ventilation was an indication for pECLA. The pECLA consisted of a polymethylpentene

oxygenator with heparin coating and a membrane surface area of 1.3 m^2 (iLA Membrane Lung→, Xenios AG, Heilbronn, Germany). Filling volume was 250 ml. The cannulas were inserted in the femoral artery (13 or 15 Fr) and in the femoral vein (15 or 17 Fr). pECLA initiation and therapy was performed according to the manufacturer's instructions of use and local standards.

The collected data contained origin of ARDS at ICU admission, demographic parameters such as age, sex, height, weight, diseases, hours of ventilation before pECLA initiation, and SOFA score before pECLA. Furthermore, subjects were retrospectively classified in PRESERVE and RESP scores according to the work of Schmidt et al. (1, 2). We recorded ventilator settings with airway pressures (peak/plateau inspiratory pressure, PEEP, driving pressure) and tidal volume. As all patients were ventilated in a pressure controlled mode peak inspiratory pressure and plateau pressure were equal. Registered hemodynamic parameters were mean arterial pressure (MAP), central venous pressure, heart rate, and norepinephrine dose per minute, and additionally, blood gas measurement with Horowitz index (P_{aO2}/F_{IO2}), P_{aCO2}, pH, and S_{aO2}. All parameters were registered straight before pECLA initiation, as well as 2 and 24 hours after pECLA initiation. Calculating the scores required specific additional information, such as laboratory values, organ function, comorbidity, medication, and specific interventions before pECLA initiation.

For statistical analysis, data are presented as mean and standard deviation (mean ± SD). After confirmation of normal distribution with the Kolmogorov–Smirnov test, significance was tested within groups with repeated-measures ANOVA with post-test and between groups with unpaired t-test (InStat version 3.06, GraphPad, San Diego, CA, USA). A value of $p < 0.05$ was considered statistically significant. With GraphPad Prism 7 (GraphPad, San Diego, CA, USA) receiver operating characteristic (ROC) curves of the scores were calculated and an optimum threshold was defined by calculating the maximum Youden index (J = Sensitivity + Specifity − 1).

Results

Between 2002 and 2016 79 ARDS patients were treated with pECLA at RWTH Aachen University Hospital. After retrospective screening six patients were excluded due to missing data. 73 subjects were included with 28 women and 45 men, mean age was 51 ± 17 years (Table 1). The average SOFA score at ICU admission was 9 ± 3, mean BMI was 27.6 ± 6.1 kg/m^2. Table 1 demonstrates origin of ARDS in detail. 13 subjects had an immunocompromised status, defined as hematologic malignancies, solid tumor, solid organ transplantation, human immunodeficiency virus, or liver cirrhosis. Mean P_{aO2}/F_{IO2} was 128 ± 62 mmHg before initiation of pECLA therapy and the PEEP was at least 5 cm H_2O. All subjects fulfilled the ARDS criteria according to the Berlin definition (22). 40 subjects had a Horowitz index between 100 mmHg and 200 mmHg indicating moderate, 24 had a Horowitz index ≤ 100 mmHg indicating severe ARDS. 52 had a severe hypercapnia with a $P_{aCO2} \geq 60$ mmHg and 28 a severe acidosis with a $pH < 7.2$. All subjects were sedated and mechanically ventilated in a pressure controlled mode. Before pECLA initiation, neuromuscular blockade was not used, but 15% received inhaled nitric oxide and 14% prone position. Invasive mechanical ventilation was initiated 8 ± 8 d (range 1–33 days) before pECLA start.

Table 1
Patient characteristics before pECLA initiation for total number of patients and subgroup for survival/non-survival to hospital discharge.

Characteristics, n (%)	Total (n = 73)	Survivor (n = 37)	Non-Survivor (n = 36)
female sex	28 (38)	18 (49)	10 (28)
age, years	51 +/- 17	44 +/-15*	57 +/- 16*
Body mass index, kg/m^2	27.6 +/- 6.1	28.2 +/- 6.8	27.0 +/- 5.2
SOFA score	9 +/- 3	8 +/- 3†	10 +/- 4†
immunocompromised status	13 (18)	2 (5)*	11 (31)*
Origin of ARDS, n (%)			
pneumonia	44 (60)	25 (68)	19 (53)
viral	10 (14)	7 (19)	3 (8)
bacterial	29 (40)	14 (38)	15 (42)
aspiration	3 (4)	3 (8)	0 (0)
trauma and burn	10 (14)	5 (14)	5 (14)
status asthmaticus	3 (4)	2 (5)	1 (3)
other	16 (22)	5 (14)	11 (31)
Ventilator/pECLA therapy			
Duration of mechanical ventilation before pECLA, days	8 +/- 8	6 +/- 7†	10 +/- 10†
Duration of pECLA therapy, days	8 +/- 8	7 +/- 5	9 +/- 9
rescue therapy (ECMO)	9 (12)	5 (14)	4 (11)
Rescue therapy before pECLA			
Inhaled nitric oxide	11 (15)	7 (19)	4 (11)
neuromuscular blockade agents	0 (0)	0 (0)	0 (0)
prone position	10 (14)	4 (11)	6 (17)
Age, years			
18–49	31 (43)	22 (59)	9 (25)
50–59	14 (19)	8 (22)	6 (17)
≥ 60	28 (38)	7 (19)	21 (58)
Data presented as mean ± SD or number (n) with percent of total patient number (%).			
* $p < 0.01$ alive vs. dead, † $p < 0.05$ alive vs. dead.			

Running time of pECLA was 8 ± 8 d (range 1–53 days), and nine subjects (12%) had to be transferred from pECLA to veno-venous ECMO as a salvage therapy. Overall hospital mortality rate was 49%, but demonstrated age-related differences (< 50 years 29%, 50–59 years 43% and ≥ 60 years 75%). Subjects who died in hospital were significantly older (57 ± 16 versus 44 ± 15 years, $p < 0.001$).

Ventilation, oxygenation, acid-base status, and hemodynamics are presented before initiation of pECLA, after 2 and after 24 h in Table 2. After starting pECLA therapy a significant reduction of inspiratory pressure and driving pressure was observed in all subjects. Tidal volume was significantly reduced only 2 hours after onset, but not after 24 hours. After 24 hours significant reduction of tidal volume was only achieved for the non-surviving cohort. Blood gas analysis before pECLA initiation revealed pH 7.23 ± 0.14, P_{aCO2} 79.4 ± 30.6 mmHg, S_{aO2} 94.6 ± 4.8% and P_{aO2}/F_{IO2} 126 ± 59 mmHg. After 2 and 24 hours of pECLA P_{aCO2} was significantly reduced and pre-pECLA acidosis was compensated in all subjects. Significant rise of S_{aO2} succeeded not until 24 hours and not for the

non-surviving cohort. Significant differences between the surviving and non-surviving cohort have been detected in P_{aCO2} after 24 hours and P_{aO2}/F_{IO2} after 2 and 24 hours. A significant increase of oxygenation index was achieved after 2 hours, but remained significantly increased after 24 hours only for the surviving cohort. Overall pECLA therapy achieved a stabilization of cardiovascular parameters such as heart ratio, mean arterial pressure, and central venous pressure (Table 2). MAP significantly increased without change of norepinephrine dose for all subjects after 24 hours, for the surviving cohort even after 2 hours.

Table 2
Ventilator settings, blood gas analysis, and hemodynamic parameters before, 2 and 24 hours after pECLA initiation.

	Before pECLA			2 hours after pECLA start			24 hours after pECLA start		
	all (n = 73)	survivor (n = 37)	non-survivor (n = 36)	all (n = 73)	survivor (n = 37)	non-survivor (n = 36)	all (n = 73)	survivor (n = 37)	non-survivo (n = 36)
Ventilation									
peak pressure, mbar	32.7+/-6.2	32.6+/-7.0	32.6+/-5.2	30.4+/-5.4*	31.4+/-6.1	30.4+/-4.5*	29.4+/-4.3†	29.1+/-4.4†	29.9+/-4.3
plateau pressure, mbar	32.7+/-6.2	32.6+/-7.0	32.6+/-5.2	30.4+/-5.4*	31.4+/-6.1	30.4+/-4.5*	29.4+/-4.3†	29.1+/-4.4†	29.9+/-4.3
PEEP, mbar	13.7+/-4.1	13.6+/-5.2	12.8+/-4.7	14.4+/-3.8	14.9+/-4.2	13.3+/-4.6	13.7+/-3.9	13.7+/-5.1	12.9+/-4.7
driving pressure, mbar	19.0+/-5.6	18.7+/-6.4	19.0+/-4.6	16.2+/-4.6*	16.4+/-5.1*	16.3+/-4.4*	15.5+/-4.2†	15.8+/-4.7†	16.2+/-4.3
T_V per kg bodyweight, ml/kg	4.8+/-1.6	4.3+/-2.0	4.5+/-1.6	4.1+/-1.2*	3.8+/-1.3	3.8+/-0.8*	4.4+/-1.5	4.3+/-1.7	3.7+/-1.2†
Blood gas analysis									
pH	7.23+/-0.14	7.24+/-0.14	7.21+/-0.15	7.37+/-0.12*	7.39+/-0.12*	7.35+/-0.12*	7.40+/-0.10†	7.42+/-0.08†	7.37+/-0.1
P_{aCO2}, mmHg	79.4+/-30.6	74.6+/-25.7	85.9+/-34.9	51.7+/-11.0*	49.9+/-10.4*	53.7+/-11.5*	48.6+/-11.6†	45.1+/-11.4†‡	50.9+/-13.
S_{aO2}, %	94.6+/-4.8	94.4+/-5.7	94.6+/-3.6	95.6+/-3.1	95.1+/-6.6	94.9+/-2.2	96.3+/-2.4†	96.6+/-2.1†	95.8+/-2.7
P_{aO2}/F_{IO2}, mmHg	126+/-59	132 +/-75	124+/-47	107+/-59*	123+/-73*‡	90+/-30*‡	136+/-54	151+/-49†‡	120+/-54‡
Hemodynamics									
heart rate, bpm	103+/-22	100+/-23	104+/-23	96+/-21	95+/-21	99+/-22	92+/-19†	93+/-19	91+/-20†
MAP, mmHg	76+/-14	76+/-11	77+/-13	80+/-14*	81+/-8*	80+/-13	83+/-13†	83+/-13†	83+/-14†
CVP, mmHg	16+/-5	15+/-4	16+/-5	15+/-5	14+/-5	16+/-6	14+/-4	15+/-4	14+/-5
norepinephrine, µg/kg/min	0.26+/-0.35	0.22+/-0.24	0.30+/-0.44	0.28+/-0.50	0.21+/-0.23	0.37+/-0.69	0.25+/-0.51	0.17+/-0.25	0.34+/-0.6
Abbreviations used for positive end expiratory pressure (PEEP), tidal volume (T_V), arterial partial pressure of carbon dioxide (P_{aCO2}), arterial oxygen saturation (S_{aO2}), horowitz index (P_{aO2}/F_{IO2}), mean arterial pressure (MAP) and central venous pressure (CVP).									
Data presented as mean ± SD, * $p < 0.05$ before vs. 2 h, † $p < 0.05$ before vs. 24 h, ‡ $p < 0.05$ alive vs. dead.									

For all subjects RESP, PRESERVE and SOFA scores were calculated at initiation of pECLA. Mean score of alive versus deceased subjects was 3 ± 1 versus − 1 ± 1 for RESP score ($p < 0.001$), 3 ± 0 versus 6 ± 0 for PRESERVE score ($p < 0.0001$) and 8 ± 1 versus 10 ± 1 for SOFA score ($p < 0.05$). Calculation of the ROC curves (Fig. 1) demonstrated an area under the curve (AUC) of 0.78 for RESP score with a 95% confidence interval (CI) of 0.67–0.89 ($p < 0.001$). PRESERVE score achieved an AUC of 0.80 with 95% CI 0.70–0.90 ($p < 0.0001$) as well as SOFA score an AUC of 0.66 with 95% CI 0.53–0.79) ($p < 0.05$). The calculation of Youden index allowed the definition of a cut-off value for RESP score of 0 (sensitivity 84%, specificity 67%), for PRESERVE score of 4 (sensitivity 73%, specificity 72%) and for SOFA score of 8 (sensitivity 76%, specificity 61%).

Discussion

RESP and PRESERVE score were validated for veno-venous ECMO in hypoxemic ARDS, but despite comparable high mortality rates specific risk scores are lacking for low-flow extracorporeal carbon dioxide elimination in hypercapnic ARDS. In our observational study PRESERVE and RESP score demonstrated a

statistically significant association with hospital mortality for extracorporeal carbon dioxide elimination during ARDS. Both scores were superior to SOFA score in our study.

In the ELSO registry, used for the RESP score definition, only 21% of the subjects had a bacterial pneumonia, and major diagnostic groups were other acute respiratory diagnosis with 28% as well as unspecified with 30% (1). Nevertheless in the recently published EOLIA ECMO trial 45% of ARDS subjects suffered from a bacterial pneumonia and 18% from viral pneumonia (23). In our study, bacterial pneumonia was also the most frequent origin of ARDS with 40% and viral pneumonia was observed in 14%. RESP and PRESERVE score development and validation showed, that age, immunocompromised status, duration of mechanical ventilation, and SOFA score are relevant risk factors for outcome of ECMO (1, 2). We observed also a significantly younger age, less immunocompromised status, shorter pre-pECLA duration of mechanical ventilation and lower SOFA score in the survivor group (Table 1). There was no direct impact of ARDS etiology to survival rate. Pre- and post-pECLA salvage therapy was not different between survivors and non-survivors. As in former pECLA studies extracorporeal CO_2 removal allowed an enhanced lung protective ventilation.

The PRESERVE score used a database of 140 ARDS subjects with ECMO to identify risk factors and to generate this score (2). Subjects presented with a median P_{aO2}/F_{IO2} of 53 mmHg (interquartile range 43–60 mmHg), a median P_{aCO2} of 63 mmHg (51–77 mmHg) and a median pH of 7.22 (7.15–7.32) before ECMO. Based on pre-ECMO assessment data of the Extracorporeal Life Support Organization Registry (ELSO) the RESP score was published 2014 using 2,355 ECMO cases from 2000 to 2012 (1). Blood gas analysis revealed similar values before ECMO initiation with a median P_{aO2}/F_{IO2} of 59 mmHg (interquartile range 48–75 mmHg), median P_{aCO2} of 56 mmHg (44–73 mmHg) and a median pH of 7.25 (7.15–7.35). In our study, subjects presented with a better oxygenation, indicated by a Horowitz index of 126 ± 59 mmHg, but with a severe respiratory acidosis (P_{aCO2} 79.4 ± 30.6 mmHg and pH 7.23 ± 0.14). Patients with a severe disturbed oxygenation comparable to the PRESERE and RESP validation studies were not suitable for pECLA due to the limited oxygen uptake. These patients were primary connected to veno-venous ECMO. Nine pECLA patients were switched to veno-venous ECMO after further deteriorating oxygenation. Nevertheless, oxygenation and acid base status were more compromised than in the prospective randomized controlled Xtravent study, which evaluated pECLA in combination with an ultraprotektive ventilation strategy compared to lung protective ventilation in severe ARDS (10).

$ECCO_2R$ therapy as arterio-venous pECLA or low-flow veno-venous device seems a promising option to ensure optimized lung protection avoiding further ventilator induced lung injury (VILI) (24) and clinical trials are ongoing (25). Although there was no leading severe hypoxemia, hospital mortality was 49% in our study compared to 43% in the RESP score study by Schmid et al. (1). Therefore, in case of extracorporeal carbon dioxide removal a specific risk score seems also useful to identify high-risk patients.

In the PRESERVE and RESP score validation study most of the included patients suffered from severe hypoxemic ARDS (1, 2), whereas only 33% of our subjects had a severe ARDS before pECLA start. In the Berlin definition of ARDS, severity of disturbed oxygenation defines the grade and correlates with mortality (14, 22). Therefore, a direct transfer of the RESP and PRESERVE score from ECMO to $ECCO_2R$ seems not suitable, because patients have different ARDS characteristics with leading hypercapnia and concomitant acidosis but without life-threatening hypoxemia. After positive validation for ARDS patients with leading hypercapnia and $ECCO_2R$ therapy the established RESP and PRESERVE scores could be used for hypoxic as well as hypercapnic ARDS patients intended for extracorporeal lung support.

Validation of pECLA in our study demonstrated comparable results to other studies analyzing PRESERVE and RESP score for veno-venous ECMO (Table 4). We additionally tested, if a non-specific SOFA score could be an alternative tool to assess the risk profile, but AUC as indicator for accuracy was lower. Nevertheless a SOFA score > 12 represents a risk factor in the PRESERVE score but not in the RESP score. Overall, only the specific scores demonstrated a good diagnostic accuracy for pECLA. Comparing both scores, the PRESERVE score requires less items and as a result seems easier to handle than the RESP score. In conclusion both scores seem suitable for pECLA as $ECCO_2R$ device.

As mentioned above several studies evaluated RESP and PRESERVE scores for other ECMO populations with differing accuracy and without superiority of one score (Table 3). Survival in the different predefined risk classes demonstrated some inconsistent results but with a generally increasing mortality for a higher risk score (Table 4). Compared to these studies the performance of PRESERVE and RESP was non-inferior for pECLA in our study. Limitations of our study are the retrospective single center design and the missing long-term survival data. A prospective registry of $ECCO_2R$ could be able to generate more detailed as well as long-term data. With our retrospective study, PRESERVE and RESP score could be sufficiently validated to identify a high-risk profile before starting an extracorporeal carbon dioxide elimination. Nevertheless, ARDS therapy and especially time of initiation and decision for conventional therapy versus $ECCO_2R$ or ECMO require clinical assessment and could not be replaced by a simple scoring.

Table 3
Comparing area under the curve (AUC) of ROC curve with 95% confidence interval (CI) for PRESERVE and RESP score in different validation studies.

study	n	treatment	PRESERVE (95% CI)	RESP (95% CI)
Schmidt (2)	140	ECMO	0.89 (0.83–0.94)	NA
Schmidt (1)	2355	ECMO	NA	0.74 (0.72–0.76)
Brunet (20)	41	ECMO	0.69 (0.53–1.87)	0.60 (0.41–0.78)
Kang (21)	99	ECMO	0.64 (0.51–0.77)	0.69 (0.58–0.81)
Klinzing (15)	51	ECMO	0.67 (0.52–0.82)	0.65 (0.50–0.80)
Lee (19)	50	ECMO	0.80 (0.66–0.90)	0.79 (0.65–0.89)
our cohort	73	pECLA	0.80 (0.70–0.90)	0.78 (0.67–0.89)

Table 4
Survival rate in percent as well as absolute number of patients according to risk classes for RESP and PRESERVE score in different validation studies.

RESP			Survival in risk classes in % (n)				
study	subjects	treatment	I	II	III	IV	V
Schmidt (1)	2355	ECMO	92 (164)	76 (563)	57 (1033)	33 (449)	18 (146)
Brunet (20)	41	ECMO	NA (0)	50 (6)	43 (14)	20 (5)	50 (2)
Huang (17)	23	ECMO	100 (2)	75 (8)	75 (4)	50 (4)	0 (5)
Hsin (18)	107	ECMO	75 (NA)	68 (NA)	63 (NA)	24 (NA)	38 (NA)
Klinzing (15)	51	ECMO	100 (3)	61 (18)	56 (23)	29 (7)	NA (0)
our cohort	73	pECLA	55 (11)	80 (15)	62 (26)	15 (13)	14 (8)

PRESERVE			Survival in risk classes in % (n)			
study	subjects	treatment	I	II	III	IV
Schmidt (2)	140	ECMO	97 (34)	79 (38)	54 (26)	16 (38)
Brunet (20)	41	ECMO	58 (12)	54 (11)	57 (7)	0 (5)
Enger (20)	304	ECMO	89 (35)	72 (90)	60 (97)	36 (67)
Klinzing (15)	51	ECMO	65 (17)	77 (13)	38 (16)	20 (5)
our cohort	73	pECLA	100 (12)	63 (24)	36 (25)	17 (12)

In our study we focused on pumpless ECLA as $ECCO_2R$ device, but other veno-venous low-flow ECLA systems are also used for hypercapnic ARDS. For veno-venous devices, there is an ongoing transition from leading decarboxylation to decarboxylation plus oxygenation with increasing blood flow. As RESP and PRESERVE were primary validated for classical high-flow ECMO and now were additionally validated for pECLA as decarboxylation device by our study, we hypothesize that these scoring systems are also suitable for other low-flow ECLA systems. Further investigations of low-flow veno-venous $ECCO_2R$ could be used to confirm this assumption.

Conclusions

Performance of both scores was at least as good for pECLA as for veno-venous ECMO, the primary validation cohort. Both scores, RESP and PRESERVE, but not SOFA score seem suitable to point out the risk profile of ARDS patients with leading hypercapnia and pECLA expanding the scope from ECMO to $ECCO_2R$.

List Of Abbreviations

ARDS Acute respiratory distress syndrome

AUC Area under the curve

CI Confidence interval

CVP Central venous pressure

$ECCO_2R$ Extracorporeal carbon dioxide removal

ECMO Extracorporeal membrane oxygenation

ELSO Extracorporeal Life Support Organization

P_{aO2}/F_{IO2} Horowitz index

MAP Mean arterial pressure

P_{aCO2} Arterial partial pressure of carbon dioxide

pECLA Pumpless extracorporeal lung assist

PEEP Positive endexpiratory pressure

PRESERVE PRedicting dEath for SEvere ARDS on VV-ECMO

RESP Respiratory ECMO survival score

ROC Receiver operating characteristic curve

S_{aO2} Arterial oxygen saturation

SOFA Sequential organ failure assessment score

T_V tidal volume

VILI Ventilator induced lung injury

Declarations

Ethics approval and consent to participate

Ethical approval was received by the RWTH Aachen University regional research ethics committee (AF 047/16) and authorized retrospective acquisition of anonymized patient data without informed consent.

Consent for publication

Not applicable.

Availability of data and materials

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

Competing interests

The authors declare that they have no competing interests.

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Author's contributions

JP designed the study, searched literature, collected as well as analyzed data and prepared the manuscript. TM did literature search, collected as well as analyzed data and prepared the manuscript, RD, NS, JA and GM contributed to the preparation of the manuscript and reviewed the manuscript, RK designed the study, searched literature, designed the study, reviewed the analyzed data, contributed to the preparation of the manuscript and reviewed as well as submitted the manuscript.

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Not applicable.

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Figures

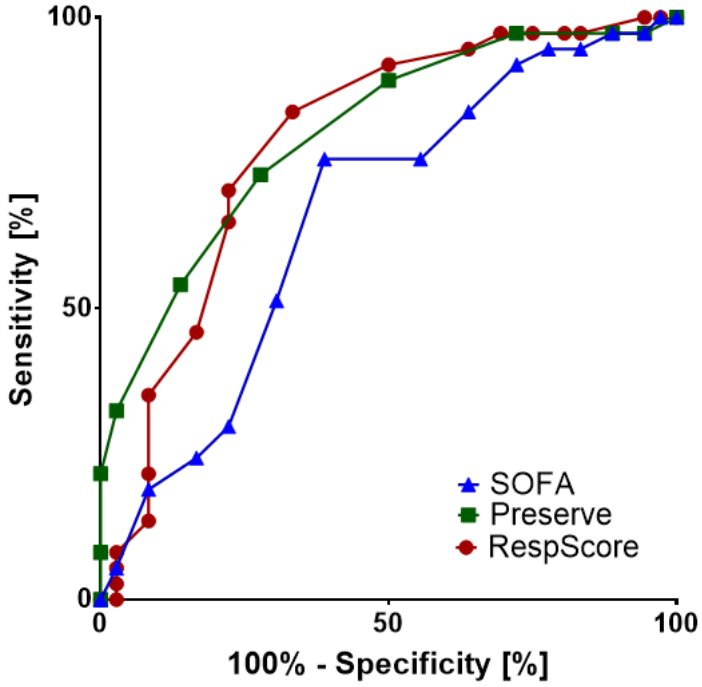

Figure 1

Receiver Operating Characteristic (ROC) curve analysis for RESP, PRESERVE, and SOFA score.