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Predictors of extracorporeal membrane oxygenation efficacy in patients with acute respiratory failure

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The purpose of this article is to describe the problem of predicting the lung function recovery in patients with extracorporeal membrane oxygenation for acute respiratory distress syndrome. Data from CESAR and EOLIA clinical trials on the efficacy of extracorporeal membrane oxygenation in patients with acute respiratory distress syndrome have been reviewed and some controversial results discussed. The prognostic PRESERVE and RESP scores developed as prognostic tools on the basis of the results of these studies, are presented, the limitations of their applicability in various forms of acute respiratory distress syndrome are discussed. We propose to subdivide the predictors of the extracorporeal

membrane oxygenation outcome in patients with acute respiratory distress syndrome into 4 following groups: 1. Lung injury severity criteria, including parameters of their lung mechanical and functional properties. 2. Time from acute respiratory failure onset to extracorporeal membrane oxygenation initiation, which reflects the rate of pathological processes in lungs and timing of decision to initiate extracorporeal membrane oxygenation. 3. The etiology of pulmonary disorders, obviously directly affecting the reversibility of pathological processes in the lungs. 4. The severity of the patient's general condition, including the severity of manifestations of multiple organ failure, the degree of decompensation of concomitant chronic diseases, including oncological and associated with immunosuppression. Several diseases are associated with a higher risk of specific complications, particularly hemorrhagic, during extracorporeal membrane oxygenation.

Keywords: extracorporeal membrane oxygenation, acute respiratory distress syndrome, acute respiratory failure

ARDS, Acute Respiratory Distress Syndrome
ARF acute respiratory failure
CT, computed tomography
ECMO, extracorporeal membrane oxygenation
FiO2, fraction of oxygen in the inspired air
ICU, Intensive Care Unit
MLV, mechanical lung ventilation
OI, oxygenation index
OSI, oxygenation saturation index
PaO_2, partial pressure of oxygen in arterial blood
PEEP, positive end-expiratory pressure
Pplat, plateau pressure
TV, tidal volume
ΔP (driving pressure), pressure difference between Pplat and PEEP

Introduction

Extracorporeal membrane oxygenation (ECMO) is a hardware-based technique of life support that allows a partial replacement of lung function in the event of extremely severe lung damage. Playing the role of prosthesis, ECMO does not have a direct therapeutic effect on the lung tissue, so, the treatment result completely depends on the reversibility of the main process in the lungs. The article reviews the literature sources describing the predictors of survival during veno-venous ECMO in patients with acute lung failure.

History of using extracorporeal membrane oxygenation in acute respiratory failure

The ECMO method is based on the use of a special polymer membrane that allows oxygenation of the venous blood flowing through the extracorporeal circuit [1]. ECMO principles were developed in the 60-s of the XX century. For a long time, this technique had been used mainly in neonatology practice. The first use of ECMO in adults dates back to 1972 [2], and the first research on this topic was made in 1979 [3]. The ECMO results of that time initially disappointed doctors and scientists.

The interest in ECMO technology revived again relatively recently, after its successful application during the H1N1 influenza pandemic that developed in 2009, when the conventional therapy - mechanical lung ventilation - turned to be ineffective [4, 5]. The ECMO success in that patient population prompted clinicians to study the efficacy of the technique in the other diseases leading to acute pulmonary failure. Currently, ECMO has found its place in the treatment of the primary pulmonary etiology diseases and the extrapulmonary ones complicated by severe respiratory failure [6]. In addition, the use of ECMO as a "bridge" to lung transplantation and for cardiopulmonary resuscitation has also

been described [7, 8]. One of the most common indications for ECMO is acute respiratory distress syndrome (ARDS). The efficacy of this technique in ARDS was evaluated in CESAR [9] and EOLIA [7] studies. The CESAR study showed a significant reduction of a 90-day mortality in the ECMO group. The EOLIA study showed no statistically significant intergroup difference, despite the fact that the mortality in the ECMO group was 13% lower than in the comparison group. It is worthwhile to note that both studies had significant limitations that may have influenced the results. For example, in the CESAR study, some patients from the ECMO group received conventional therapy, while there was no standardization of mechanical lung ventilation (MLV) parameters in the comparison group. The EOLIA study was terminated upon reaching 75% of the maximum sample, 28% of patients with refractory hypoxemia from the comparison group were transferred to the ECMO group. In addition, the authors suggested that the study was not powerful enough to meet the original goal of demonstrating a 20% difference in mortality between ECMO and comparison groups. At the same time, data from a meta-analysis carried out on the basis of the retrospective clinical studies CESAR and EOLIA, as well as three other observational studies, indicated a decrease in mortality when using ECMO in patients with severe ARDS [10]. In general, the inconsistency of the data obtained did not allow making an unambiguous conclusion regarding the benefits of ECMO for patients.

Predictive scores for the extracorporeal membrane oxygenation efficacy

ECMO is a complex and expensive technique, while it can be accompanied by a number of serious complications [11]. Therefore,

before its use, it is necessary to evaluate the criteria for the reversibility of lung injury and the prognosis of the disease as a whole.

To solve this problem, the prognostic PRESERVE score (2013) (Table 1) [12] and RESP score (2014) (Table 2) [13] were proposed. The PRESERVE score is based on the analysis of 140 patients with ARDS who underwent ECMO in the period from 2008 to 2012. The MLV parameters (Pplat, FiO_2, (positive end-expiratory pressure [PEEP], tidal volume [TV], driving pressure), lung function (compliance, PaO_2/FiO_2 ratio, arterial blood saturation) were assessed, as well as the parameters of the acid-base status, the treatment measures taken, time intervals (from admission to transfer to the intensive care unit (ICU), from admission to the ECMO start, from transfer to the ICU to the ECMO start, from the initiation of mechanical ventilation to the ECMO start). Based on the correlation of the above factors with mortality, a Scoring tool was proposed containing 7 criteria: age (under 45, 45–55, over 55 years), body mass index over 30, immunocompromised status, SOFA score exceeding 12, mechanical ventilation duration for over 6 days, prone positioning before ECMO, PEEP lower 10 cm H_2O and Pplat more than 30 cm H_2O. However, some parameters, such as compliance, which had been shown to be correlated with survival, were not included in the final criteria of the Score.

Table 1. Parameters used in the PRESERVE score and their corresponding scoring points

Parameter	Scoring points
Age, years	
< 45	0
45–55	2
> 55	3
Body Mass Index > 30	-2
Ummunocompromised	2

SOFA score > 12	1
MLV for > 6 days	1
No prone positioning before ECMO	1
PEEP < 10 cm H_2O	2
Plateau pressure > 30 cm H_2O	2
Total Score	**0–14**

RESP Score (Table 2; Figure) is based on the analysis of 2,355 patients from the ELSO registry who underwent ECMO for ARDS from 2000 to 2012. The criteria to be included in the RESP Score were determined based on the regression analysis of ARDS etiology, ventilation regimens and arterial blood pCO_2 before the ECMO start, as well as associated pathology, ECMO parameters, treatment measures undertaken, and patient age in the groups of survived and non-survived patients.

Table 2. Parameters used in the RESP score and their corresponding scoring points

Parameter	Scoring points
Age, years	
18–49	0
50–59	-2
≥ 60	-3
Immunocompromised status	-2
Mechanical ventilation prior to initiation of ECMO	
<48 hours	3
48 hours - 7 days	1
>7 days	0
Acute Respiratory diagnosis group (*Choose one*)	
Viral pneumonia	3
Bacterial pneumonia	3
Bronchial asthma	11
Trauma/burn	3

Aspiration pneumonitis	5
Other acute respiratory diagnosis	1
Non-respiratory or chronic respiratory diagnosis	0
Central nervous system dysfunction	-7
Acute associated (non-pulmonary) infection	-3
Neuro-muscular blockade before ECMO	1
Nitric oxide use before ECMO	-1
Bicarbonate infusion before ECMO	-2
Cardiac arrest before ECMO	-2
$PaCO_2$, mm Hg	
< 75 mm Hg	0
≥75 mm Hg	-1
Peak inspiratory pressure, cm H_2O	
< 42 cm H_2O	0
≥42 cm H_2O	-1
Total RESP Score	**-22 – 15**

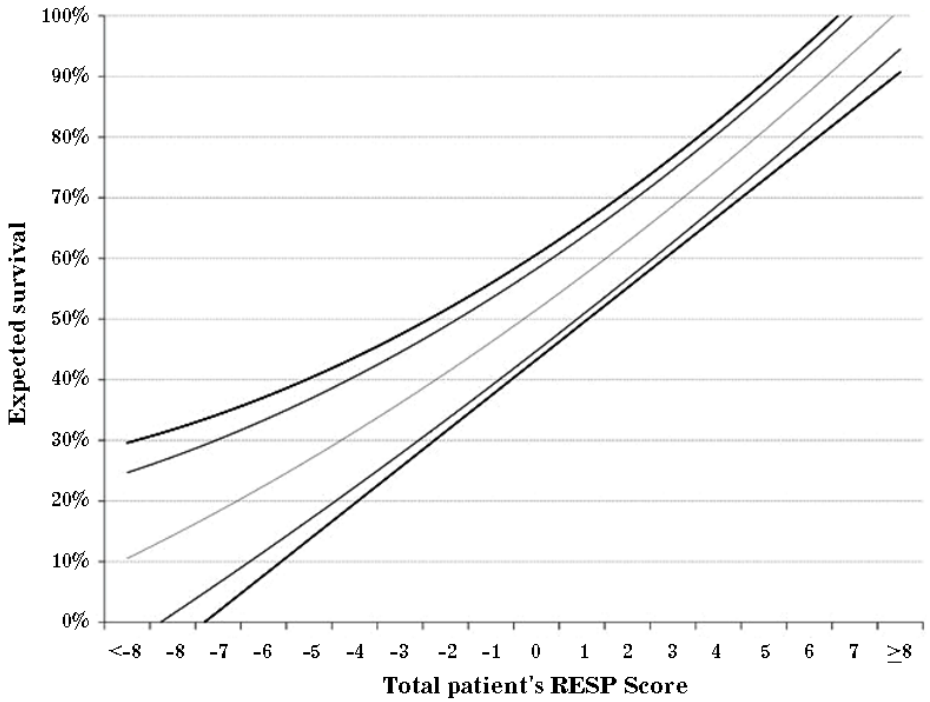

Figure. Expected survival depending on the total RESP score; light-gray lines denote the limits of the 95% confidence interval; dark gray lines denote the limits of 99% confidence interval

Of all available Scoring tools, the RESP Score was developed based on the analysis of the largest patient sample size. However, in authors' opinion, this may be a methodological limitation, since over recent 12 years a new generation of ECMO devices has appeared and the tactics of treating ARDS patients has changed, which could have affected the uniformity of the sample. On the other hand, two thirds of patients were included in the study after 2009, which may reduce the bias related to the study duration.

ECMO guidelines such as ELSO Guidelines for Adult Respiratory Failure [14], ECMO In The Adult Patient [15], Extracorporeal Life Support For Adults [16] stress the importance of assessing the disease prognosis. Incurable conditions, such as irreversible brain damage and terminal cancer, have been claimed as obvious predictors of a poor outcome.

Predictive criteria of survival in extracorporeal membrane oxygenation

The predictive criteria of survival can be subdivided into 4 groups:

1. The lung injury severity.
2. Time factors for the acute respiratory failure development and the ECMO onset.
3. Etiology of pulmonary disorders.
4. The severity of patient's general condition.

The lung injury severity

The criteria of the pulmonary parenchyma injury severity include the lung oxygen-delivery function parameters and the respiratory mechanics parameters indicating the lung tissue compliance.

The severity of impaired oxygen transport function in the lungs is the main indication for starting an ECMO procedure. ECMO guidelines [14-17], research protocols [7, 9] and recommendations for the ARDS treatment [18] in their section "Indications for ECMO" define the PaO_2/FiO_2 ratio, which reflects the hypoxemia severity, as being the most common and easy-to-use criterion for the assessment of the pulmonary injury severity. To obtain more reliable data on the respiratory failure severity, it is recommended to assess the PaO_2/FiO_2 ratio over time: at admission and after 24 hours [19]. The PaO_2/FiO_2 ratio is also present as one of the criteria in the APPS score proposed by J. Villar et al. to predict the outcome of the disease in patients with ARDS [20]. For the same purpose, it was proposed to use a modification of the PaO_2/FiO_2 ratio i.e. the oxygenation index (OI), which includes, in addition to the PaO_2 and FiO_2 parameters, the mean airway pressure. The OI was developed in 1988 to determine the indications for ECMO in neonates with RDS [21], but proved to be applicable to predict mortality in ARF and in the adult population [22]. Another parameter, an Oxygenation saturation index (OSI), is a modified SpO_2/FiO_2 index and also takes into account the mean airway pressure. The OSI correlation with mortality in ARDS patients has been proven [23].

Lung Injury Score (LIS) proposed by J.F. Murray et al. [24] in 1988 was also investigated as a predictive model. However, the results obtained do not allow using LIS to predict outcomes due to its low sensitivity [25]. The comparison of PaO_2/FiO_2, SpO_2/FiO_2, OI, OSI, and Murray LIS score was made in the VALID study, which demonstrated a correlation between OI and OSI, both indices being found higher in non-survived patients, but a significant relationship was demonstrated only for OSI. Meantime, PaO_2/FiO_2, SpO_2/FiO_2, OI, and Murray LIS were not independent predictors of mortality [26].

However, it should be emphasized that the severity of parenchymal pulmonary disorders, although being an unfavourable prognosis criterion, does not indicate the irreversible nature of the injury and is never considered a contraindication to the ECMO start.

When developing the PRESERVE score, no association was generally shown between survival and PaO_2/FiO_2 at the time of ECMO initiation.

The mechanical properties of the lung tissue, primarily static compliance, are the most important characteristics of lung status and can probably serve as a predictive criterion of the pathological process reversibility. Only two studies evaluated the respiratory system compliance as an independent parameter; in the PRESERVE study, the pulmonary compliance median values in the survivor group were significantly higher: 19 in the survivor group and 16 in the non-survivor group; the M. Schmidt study in 2019 [27] also showed a correlation of a higher lung compliance with the survival.

Other studies do not mention lung compliance as a predictive criterion, but note that the use of "hard" ventilation modes is an unfavourable sign. In a study by L. Munshi et al., MLV with peak pressure above 30 cm H_2O was considered as an additional factor of the lung tissue damage and, if lasted for over 7 days, was considered a contraindication for the ECMO initiation [10].

In the studies of mechanical ventilation for ARDS, there is a lot of evidence that the high inspiratory pressure, ΔP (driving pressure), correlate with a worse outcome of the disease [28, 29]. The limits of safe mechanical ventilation have been considered a TV of 6 mL/kg of an ideal body weight, ΔP of no more than 15 cm H_2O and a peak inspiratory pressure of no more than 30 cm H_2O [30].

However, the use of "non-protective" ventilation modes is not always a doctor's error. The use of a high inspiratory pressure, high "driving pressure" can be dictated by impaired mechanical properties of the lungs, in particular a decreased compliance of the lung tissue. In this context, the causal relationships remain unclear: either the use of "non-protective" ventilation modes leads to lung injury, or the primary impairment of the lung tissue compliance makes to use a high inspiratory pressure and "driving pressure". One and the same TV considered to be “protective” (6 mL/kg of an ideal body weight) can be obtained with different “driving pressures”, depending on the compliance of the patient's respiratory system. If the compliance is moderately reduced, a safe driving pressure of 15 cm H_2O or lower will be ensured, however, in case of marked restrictive disorders, the same, formally protective TV will be provided only with a significant excess of both the "driving pressure" and the peak inspiratory pressure at Pressure control or plateau pressure Volume control.

According to M.B. Amato et al., a decrease in TV and an increase in PEEP resulted in better outcomes only if they were associated with a decrease in ΔP [31].

That is, the TV assessment in the context of protective ventilation makes one to judge reliably on the relationship of TV to the survival and the mechanical lung ventilation safety only if the lung compliance is having been considered.

In the study of 56 patients who received ECMO for parenchymal lung failure, H.S. Kim et al. demonstrated that the driving pressure before ECMO was significantly higher in the group of patients with poor outcome, than in survivals [32]. Meantime, the lung compliance parameters were also assessed in both groups before and during ECMO, and the compliance appeared higher both before ECMO and during

mechanical ventilation with ECMO in survivals. Similar results were obtained by M. Schmidt et al. and LIFEGARDS group in a joint study where lower lung compliance at ECMO initiation was associated with a worse outcome [27]. However, the same study did not show any statistically significant differences between survivals and non-survivals in lung compliance values on initial 2 days on ECMO. Perhaps that was due to a decrease in the lung compliance after the start of lung protective ventilation during ECMO. This hypothesis found its confirmation in the study by H. Roze et al. that in 2016 demonstrated a decrease in thoracic pulmonary compliance in the first 24 hours after the start of lung protective ventilation [33]. The authors related the obtained results to a possible de-recruitment of the lungs due to a decreased TV and suggested increasing PEEP in order to prevent lung de-recruitment in response to artificial decrease in TV.

A similar conclusion can be drawn on the basis of the study of A.J. Walkey; its results indicated that in patients with ARDS, the combination of high PEEP values and low TV was associated with a better outcome than in patients with low TV and PEEP [34].

Summarizing all of the above, we can assume that it is the value of the respiratory system compliance, rather than a separate assessment of the plateau pressure (Pinsp), “driving pressure” and TV, that can *reflect the actual severity of lung injury* and serve as a predicting criterion of ECMO prospects.

According to the literature, a computed tomography (CT) is one of the main instrumental tools for the diagnosis of lung parenchymal diseases; however, there are few data on the use of CT results for predictive purposes. K. Ichikado et al. have indicated that the presence of pulmonary fibrosis signs at CT in the first week after the ARDS onset is an independent predictor of mortality [35]. Similar results were obtained

by J.H. Chung et al., According to their data, the fibrosis signs on CT scan, damage to more than 80% of the lung tissue, and the signs of an increased pressure in the right cardiac chambers (based on the CT signs consistent with pulmonary artery dilatation and increased volume of the right ventricle) are the predictors of poor outcome [36].

Timing of starting the extracorporeal membrane oxygenation

Almost all studies and recommendations indicate that an earlier ECMO start leads to better results. Moreover, not only the decision making time from the development of critical hypoxia to the activation of ECMO is estimated, but also the total time from the onset of the disease to the development of severe ARDS. And if the best result in case of a quick decision-taking is quite understandable, then the causes of the worst result in case of a slow or delayed development of the pathological process require further studying and understanding.

One of the key criteria for ARDS diagnosis, according to Berlin definition, is the time for symptoms to develop: no more than 7 days. [37]. At the same time, the authors of the RESP score proposed to consider the duration of mechanical lung ventilation before the start of ECMO less than 48 hours as one of the predictors of a favourable outcome. Thus, a slower progression of the disease per se is prognostically an unfavourable criterion and may delay taking the decision to start ECMO.

It should also be noted that the timing of ARDS development is considered as a prognostic factor outside the ECMO context. According to Z. Ruyang et al. and R. Zhang et al. [38, 39], a later onset of ARDS is associated with a higher 28- and 60-day mortality. Meantime, a slow development of symptoms was observed in 31% of patients, they had a shorter life expectancy and higher mortality than the patients with a faster

onset of ARDS. In addition, the authors also note differences in the dynamics of lung function recovery between these groups of patients, confirming the data reported by T.J. Iwashyna [40]. T.J. Iwashyna distinguished several "trajectories" of the injury and recovery (*functional impairment and recovery)* of the lungs in ARDS: "Big Hit", "Slow Burn", and the recurrent course almost indistinguishable from the previous version. The Big Hit trajectory is typical for patients with the fast development of ARDS manifested by a rapid loss of the lung function that subsequently is gradually recovering. "Slow Burn" is the lung function only moderately reduced initially that progressively decreases with the disease progression, leading to a worse outcome; this option is characteristic of a slow ARDS development.

The etiology of acute respiratory failure is mentioned in the guidelines as a possible criterion for assessing the likelihood of an adverse outcome. The causes of the ARF development are considered in the RESP score [13] proposed for the outcome prediction in patients with ARF and, according to some authors, being the most reliable of the proposed scoring tools [41]. The following diseases most often leading to ARF have been considered: viral and bacterial pneumonia, asthma, trauma and burns, aspiration pneumonitis, and others. Each nosology or group of diseases corresponds to a certain number of points (the score). For example, status asthmaticus is considered a more reversible condition than bacterial pneumonia, which indicates a better prognosis.

Sepsis is often associated with the development of ARF, including ARDS. Meantime, the data of a few studies do not allow making an unambiguous conclusion about the ECMO efficacy in the ARDS caused by sepsis. N. Nessler et al. investigated the results of ECMO use in patients with intra-abdominal purulent process where the ECMO efficacy

was not proven [42]. S. Takauji et al. demonstrated the ECMO efficacy in ARF caused by pneumonia, however, in patients with ARF caused by sepsis of extrapulmonary etiology, no benefit of ECMO was shown [43].

None of the respiratory failure causes, even of those ones mentioned as irreversible (for example, pulmonary fibrosis, emphysema, etc.) is an absolute contraindication to ECMO. The attending physician is requested to decide on one's own on the ECMO appropriateness, weighing the likelihood of a favourable outcome and the possibility of restoring the lung function [14].

The overall severity of patient's condition can also determine the outcome in patients with ARF. Severe concomitant diseases in the form of incurable conditions, for example, severe irreversible brain damage or end-stage malignant process, are absolute contraindications to ECMO due to an obvious unfavourable prognosis. The use of ECMO for some other diseases may be limited by the peculiarities of the method. Thus, during ECMO, heparinization is required because of the increased likelihood of thrombi formation caused by blood circulation in the extracorporeal circuit [11]. Therefore, the presence of a severe combined trauma or intracranial hemorrhage in a patient may be a contraindication to ECMO.

Meanwhile, the authors of some recommendations are inclined to expand the list of concomitant diseases that are contraindications to ECMO, for example, in the recommendations for ECMO published by the University of Wisconsin, the absolute contraindications include multiple organ failure with dysfunction of more than three organ systems, aortic dissection, severe aortic regurgitation; a liver failure has been referred to relative contraindications [17]. The criteria reflecting the overall severity of the disease are used in the above mentioned Scoring tools. Among the parameters assessed by the PRESERVE Score, there is

the SOFA score. The RESP Score takes into account the central nervous system dysfunction and the previous history of circulatory arrest.

According to A. Roch et al., The SOFA score can be used as a criterion for "an accurate assessment of the risk of death in patients with ARDS" [44].

Immune system disorders appear negative predictive criteria in the RESP and PRESERVE Scores. In the ELSO guidelines, a relative contraindication to ECMO is considered the immunosuppression and related neutropenia lower 400/mm^3.

Conclusion

Despite the increasing rate of using the veno-venous extracorporeal membrane oxygenation for the treatment of acute respiratory failure, the issue of predicting the outcome of the disease remains controversial. The absolute and relative contraindications for extracorporeal membrane oxygenation associated with the underlying disease and co-morbidities vary between different guidelines. At the moment, many predictive Scores and criteria have been proposed, but the data on the feasibility of using some of them are contradictory.

Most of the recommendations analyze indirect criteria of severity, such as the patient's age, the disease duration, concomitant diseases, but provide no detailed analysis of the lung condition.

The lack of generally accepted criteria for the reversibility of the pathological process in the lungs significantly complicates the assessment of the benefit-to-risk ratio when deciding whether to start extracorporeal membrane oxygenation.

References

1. Evseev AK, Zhuravel SV, Alentiev AYu, Goroncharovskaya IV, Petrikov SS. Membranes in extracorporeal blood oxygenation technology. *Membranes and Membrane Technologies.* 2019;1(4):201–211. https://doi.org/10.1134/S2517751619040024

2. Hill JD, O'Brien TG, Murray JJ, Dontigny L, Bramson ML, Osborn JJ, et al. Prolonged extracorporeal oxygenation for acute post-traumatic respiratory failure (shock-lung syndrome). Use of the Bramson membrane lung. *N Engl J Med.* 1972;286(12):629–634. PMID: 5060491 https://doi.org/10.1056/NEJM197203232861204

3. Zapol WM, Snider MT, Hill JD, Fallat RJ, Bartlett RH, Edmunds LH, et al. Extracorporeal membrane oxygenation in severe acute respiratory failure: a randomized prospective study. *JAMA.* 1979;242(20):2193–2196. PMID: 490805 https://doi.org/10.1001/jama.242.20.2193

4. Davies A, Jones D, Bailey M, Beca J, Bellomo R, Blackwell N, et al. Extracorporeal membrane oxygenation for 2009 influenza A (H1N1) acute respiratory distress syndrome. *JAMA.* 2009;302(17):1888–1895. PMID: 19822628 https://doi.org/10.1001/jama.2009.1535

5. Noah MA, Peek GJ, Finney SJ, Griffiths MJ, Harrison DA, Grieve R, et al. Referral to an extracorporeal membrane oxygenation center and mortality among patients with severe 2009 influenza A(H1N1). JAMA. 2011;306(15):1659–1668. PMID: 21976615 https://doi.org/10.1001/jama.2011.1471

6. Zhuravel SV, Kosolapov DA, Ketskalo MV. The organization of extracorporeal membrane oxygenation programs for acute respiratory failure in adult patients in a multidisciplinary hospital. Review of experience in Regensburg (Germany). *Transplantologiya. The Russian Journal of Transplantation.* 2014;(4):28–32. (In Russ.).

7. Combes A, Hajage D, Capellier G, Demoule A, Lavoué S, Guervilly C, et al. Extracorporeal membrane oxygenation for severe acute respiratory distress syndrome. *N Engl J Med.* 2018;378(21):1965–1975. PMID: 29791822 https://doi.org/10.1056/NEJMoa1800385

8. Kurilova OA, Zhuravel SV, Romanov AA, Marinin PN, Tsurova DKh, Kallagov TE, et al. Experience with application of extracorporeal membrane oxygenation in double lung transplantation. *Russian Journal of Transplantology and Artificial Organs.* 2014;(2):66–74. (In Russ.). https://doi.org/10.15825/1995-1191-2014-2-66-74

9. Peek GJ, Mugford M, Tiruvoipati R, Wilson A, Allen E, Thalanany MM, et al. Efficacy and economic assessment of conventional ventilatory support versus extracorporeal membrane oxygenation for severe adult respiratory fa-ilure (CESAR): a multicentre randomised controlled trial. *Lancet.* 2009;374:1351–1363. PMID: 19762075 https://doi.org/10.1016/S0140-6736(09)61069-2

10. Munshi L, Walkey A, Goligher E, Pham T, Uleryk EM, Fan E. Venovenous extracorporeal membrane oxygenation for acute respiratory distress syndrome: a systematic review and meta-analysis. *Lancet Respir Med.* 2019;7(2):163–172. PMID: 30642776 https://doi.org/10.1016/S2213-2600(18)30452-1

11. Bakharev SA, Popugaev KA, Kiselev KV, Samoylov AS, Udalov YuD, Zhangazinov AL, et al. Mechanisms of hemorrhagic complications during extracorporeal membrane oxygenation. A pilot study. *Russian Journal of Anaesthesiology and Reanimatology = Anesteziologiya i reanimatologiya.* 2020;(1):25–34. (In Russ.). https://doi.org/10.17116/anaesthesiology202001125

12. Schmidt M, Zogheib E, Rozé H, Repesse X, Lebreton G, Luyt CE. The PRESERVE mortality risk score and analysis of long-term outcomes after extracorporeal membrane oxygenation for severe acute

respiratory distress syndrome. *Intensive Care Med.* 2013;39(10):1704–1713. PMID: 23907497 https://doi.org/10.1007/s00134-013-3037-2

13. Schmidt M, Bailey M, Sheldrake J, Hodgson C, Aubron C, Rycus PT, et al. Predicting survival after extracorporeal membrane oxygenation for severe acute respiratory failure. The Respiratory extracorporeal membrane oxygenation survival prediction (RESP) Score. *Am J Respir Crit Care Med.* 2014;189(11):1374–1382. PMID: 24693864 https://doi.org/10.1164/rccm.201311-2023OC

14. *ELSO Guidelines for cardiopulmonary extracorporeal life support extracorporeal life support organization*, Version 1.4 August 2017 Ann Arbor, MI, USA. Available at: https://www.elso.org/Portals/0/ELSO%20Guidelines%20General%20All%20ECLS%20Version%201_4.pdf [Accessed March 23, 2019]

15. Sladen RN. ECMO in the adult patient, core critical care. *Anesthesia Analgesia.* 2018;126(2):713. https://doi.org/10.1213/ANE.0000000000002675

16. Sangalli F, Patroniti N, Pesenti A. (eds.) *ECMO-Extracorporeal life support in adults.* Switzerland AG: Springer; 2014.

17. *Extracorporeal Membrane Oxygena-tion (ECMO): Initiation and management– adult – in patient: clinical practice guideline.* USA: University of Wisconsin Hospitals and Clinics Authority; 2018.

18. Papazian L, Aubron C, Brochard L, Chiche JD, Combes A, Dreyfuss D, et al. Formal guidelines: management of acute respiratory distress syndrome. *Ann Intensive Care.* 2019;9(1):69. PMID: 31197492 https://doi.org/10.1186/s13613-019-0540-9

19. Villar J, Blanco J, del Campo R, Andaluz-Ojeda D, Díaz-Domínguez FJ, Muriel A, et al. Assessment of PaO_2/FiO_2 for stratification of patients with mode-rate and severe acute respiratory

distress syndrome. *BMJ Open.* 2015;5(3):e006812. PMID: 25818272 https://doi.org/10.1136/bmjopen-2014-006812

20. Villar J, Ambrós A, Soler JA, Martínez D, Ferrando C, Solano R, et al. Age, Pao_2/Fio_2, and plateau pressure score: a proposal for a simple outcome score in patients with the acute respiratory distress syndrome. *Crit Care Med.* 2016;44(7):1361–1369. PMID: 27035239 https://doi.org/10.1097/CCM.0000000000001653

21. Heiss KF, Bartlett RH. Extracorporeal membrane oxygenation: an experimental protocol becomes a clinical service. *Adv Pediatr.* 1989;36:117–136. PMID: 2675567

22. Dechert RE, Park PK, Bartlett RH. Evaluation of the oxygenation index in adult respiratory failure. *J Trauma Acute Care Surg.* 2014;76(2):469–473. PMID: 24458052 https://doi.org/10.1097/TA.0b013e3182ab0d27

23. Chen WL, Lin WT, Kung SC, Lai CC, Chao CM. The value of oxygenation saturation index in predicting the outcomes of patients with acute respiratory distress syndrome. *J Clin Med.* 2018;7(8). pii: E205. PMID: 30096809 https://doi.org/10.3390/jcm7080205

24. Murray JF, Matthay MA, Luce JM, Flick MR. An expanded definition of the adult respiratory distress syndrome. *Am Rev Respir Dis.* 1988;138(3):720–723. PMID: 3202424 https://doi.org/10.1164/ajrccm/138.3.720

25. Kangelaris KN, Calfee CS, May AK, Zhuo H, Matthay MA, Ware LB. Is there still a role for the lung injury score in the era of the Berlin definition ARDS? *Ann Intensive Care.* 2014;4(1):4. PMID: 24533450 https://doi.org/10.1186/2110-5820-4-4

26. DesPrez K, McNeil JB, Wang C, Bastarache JA, Shaver CM, Ware LB, Oxygenation saturation index predicts clinical outcomes in

ARDS. *Chest.* 2017;152(6):1151–1158. PMID: 28823812 https://doi.org/10.1016/j.chest.2017.08.002

27. Schmidt M, Pham T, Arcadipane A, Agerstrand C, Ohshimo S, Pellegrino V, et al. Mechanical ventilation management during extracorporeal membrane oxygenation for acute respiratory distress syndrome: an international multicenter prospective cohort. *Am J Respir Crit Care Med.* 2019;200(8):1002–1012. PMID: 31144997 https://doi.org/10.1164/rccm.201806-1094OC

28. Dreyfuss D, Soler P, Basset G, Saumon G. High inflation pressure pulmonary edema. Respective effects of high airway pressure, high tidal volume, and positive end-expiratory pressure. *Am Rev Respir Dis.* 1988;137(5):1159–1164. PMID: 3057957 https://doi.org/10.1164/ajrccm/137.5.1159

29. Gattinoni L, Pesenti A. The concept of “baby lung”. *Intensive Care Med.* 2005;31(6):776–784. PMID: 15812622 https://doi.org/10.1007/s00134-005-2627-z

30. Fan E, Del Sorbo L, Goligher EC, Hodgson CL, Munshi L, Walkey AJ, et al. An Official American thoracic society/European society of intensive care medicine/Society of critical care medicine. Clinical practice guideline: Mechanical ventilation in adult patients with acute respiratory distress syndrome. *Am J Respir Crit Care Med.* 2017;195(9):1253–1263. PMID: 28459336 https://doi.org/10.1164/rccm.201703-0548ST

31. Amato MB, Meade MO, Slutsky AS, Brochard L, Costa EL, Schoenfeld DA, et al. Driving pressure and survival in the acute respiratory distress syndrome. *N Engl J Med.* 2015;372(8):747–755. PMID: 25693014 https://doi.org/10.1056/NEJMsa1410639

32. Kim HS, Kim JH, Chung CR, Hong SB, Cho WH, Cho YJ, et al. Lung compliance and outcomes in patients with acute respiratory

distress syndrome receiving ECMO. *Ann Thorac Surg*. 2019;108(1):176–183. PMID: 30836100 https://doi.org/10.1016/j.athoracsur.2019.01.055

33. Rozé H, Doassans G, Repusseau B, Ouattara A. Decrease of thoracopulmonary compliance with pressure assist controlled ventilation in ARDS patients under ECMO and transported to a referral centre. *Intensive Care Med*. 2017;43(1):148–149. PMID: 27815586 https://doi.org/10.1007/s00134-016-4616-9

34. Walkey AJ, Goligher EC, Del Sorbo L, Hodgson CL, Adhikari NKJ, Wunsch H, et al. Low tidal volume versus non-volume-limited strategies for patients with acute respiratory distress syndrome: a systematic review and meta-analysis. *Ann Am Thorac Soc*. 2017;14(Suppl 4):S271–S279. PMID: 28846440 https://doi.org/10.1513/AnnalsATS.201704-337OT

35. Ichikado K, Suga M, Muranaka H, Gushima Y, Miyakawa H, Tsubamoto M, et al. Prediction of prognosis for acute respiratory distress syndrome with thin-section CT: validation in 44 cases. *Radiology*. 2006;238(1):321–329. PMID: 16293804 https://doi.org/10.1148/radiol.2373041515

36. Chung JH, Kradin RL, Greene RE, Shepard JA, Digumarthy SR. CT predictors of mortality in pathology confirmed ARDS. *Eur Radiol*. 2011;21(4):730–737. PMID: 20927526 https://doi.org/10.1007/s00330-010-1979-0

37. Ranieri VM, Rubenfeld GD, Thompson BT, Ferguson ND, Caldwell E, Fan E, et al. The ARDS definition task force. Acute respiratory distress syndrome: the Berlin definition. *JAMA*. 2012;307(23):2526–2533. PMID: 22797452 https://doi.org/10.1001/jama.2012.5669

38. Ruyang Z, Zhaoxi W, Yongyue W, Paula TA, Zhaozhong Z, Li S, et al. A two-stage association study identifies a high risk window of

acute respiratory distress syndrome onset time correlated with poor 28 day overall survival. A53. *Respiratory failure: risk factors and outcomes in ARDS. American Thoracic Society – 2016*, (California, San-Francisco, 13–18 may 2016). San-Francisco, 2016. Abstr A7794.

39. Zhang R, Wang Z, Tejera P, Frank AJ, Wei Y, Su L, et al. Late-onset mode-rate to severe acute respiratory distress syndrome is associated with shorter survival and higher mortality: a two-stage association study. *Intensive Care Med.* 2017;43(3):399–407. PMID: 28032130 https://doi.org/10.1007/s00134-016-4638-3

40. Iwashyna TJ. Trajectories of recovery and dysfunction after acute illness, with implications for clinical trial design. *Am J Respir Crit Care Med.* 2012;186(4):302–304. PMID: 22896591 https://doi.org/10.1164/rccm.201206-1138ED

41. Rozencwajg S, Pilcher D, Combes A, Schmidt M. Outcomes and survival prediction models for severe adult acute respiratory distress syndrome treated with extracorporeal membrane oxyge-nation. *Crit Care.* 2016;20(1):392 PMID: 27919283 https://doi.org/10.1186/s13054-016-1568-y

42. Nesseler N, Launey Y, Isslame S, Flécher E, Lebouvier T, Mallédant Y, et al. Is extracorporeal membrane oxyge-nation for severe acute respiratory distress syndrome related to intra-abdominal sepsis beneficial? *Intensive Care Med.* 2015;41(5):943–945. PMID: 25800583 https://doi.org/10.1007/s00134-015-3743-z

43. Takauji S, Hayakawa M, Ono K, Makise H. Respiratory extracorporeal membrane oxygenation for severe sepsis and septic shock in adults: a propensity score analysis in a multicenter retrospective observational study. *Acute Med Surg.* 2017;4(4):408–417. PMID: 29123901 https://doi.org/10.1002/ams2.296

44. Roch A, Hraiech S, Masson E, Grisoli D, Forel JM, Boucekine M, et al. Outcome of acute respiratory distress syndrome patients treated with extracorporeal membrane oxygenation and brought to a referral center. Intensive. *Intensive Care Med.* 2014;40(1):74-83. PMID: 24170143 https://doi.org/10.1007/s00134-013-3135-1

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