



## SYSTEMATIC REVIEW OF THE LITERATURE ON THE MEASURES USED IN EXTRACORPOREAL VENOUS-VENOUS MEMBRANE AND MECHANICAL VENTILATION AND FOR THE MANAGEMENT OF PATIENTS WITH RESPIRATORY DISTRESS SYNDROME

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### Abstract

**Objective:** To establish criteria for the management of mechanical ventilation parameters and extracorporeal venous-venous membrane for the treatment of patients with ARDS.

**Methods:** Two searches were conducted in the PubMed database, from March 29 to April 30, 2019, the process followed the PRISMA guidelines for systematic reviews and meta-analyses.

**Results:** 58 articles were identified, 5 met the inclusion and exclusion criteria. Hypercapnia was corrected with blood flow (FS) rates of 750 to 1000 ml / min and lung surface area (SP)  $\geq 0,8$  m<sup>2</sup>. The SP of 0.4 m<sup>2</sup> didn't normalize the pH, even with FS rates of 1000 ml / min. The increase in the sweep gas flow ( FGB) from 2 to 8 l / min increased the CO<sub>2</sub> removal from  $55 \pm 9$  to  $70 \pm 14$  ml / min. The passage from ECMO-VV to VMI was made with the progressive decrease of FGB from 4 to 0 l / min with constant FS.

**Conclusion:** A good elimination of CO<sub>2</sub> and oxygen supply will be achieved only when the triad of gas flow, blood flow and membrane surface is adequate.

**Keywords:** Artificial respiration; Extracorporeal membrane oxygenation; Respiratory failure, Adult respiratory distress syndrome.

### Introduction

Acute respiratory distress syndrome (ARDS) is a biologically heterogeneous clinical picture, defined as acute respiratory failure caused by acute inflammatory edema of the lung. It is a life-threatening condition where there is increased vascular permeability, followed by the entry of fluid into the

pulmonary interstitium and finally its arrival in the alveolar spaces.<sup>1–3</sup> This increases the physiological alveolar dead space, so that the alveoli are perfused but not ventilated resulting in profound hypoxemia refractory to high values of inspired oxygen fraction (FiO<sub>2</sub>).<sup>2</sup> The degree of severity of ARDS is classified around the PaO<sub>2</sub>/FiO<sub>2</sub> ratio in: Mild PaO<sub>2</sub>/FiO<sub>2</sub> ≤ 300 but > 200, Moderate PaO<sub>2</sub>/FiO<sub>2</sub> ≤ 200 but > 100 and Severe PaO<sub>2</sub>/FiO<sub>2</sub> ≤ 100.<sup>4</sup>

Although ARDS has been recognized for more than 50 years, there is no clear and effective treatment to follow to solve it, and mortality rates are still very high (50-60%).<sup>1,5</sup> A cross-sectional study of 29,144 patients enrolled in the intensive care unit (ICU) in 50 countries indicated that the prevalence of ARDS was 10.4% (3,022 patients) and, of these, 78.7% (2,377 patients) had been treated with invasive mechanical ventilation (IMV).<sup>1,6</sup> Clinical studies show that 5% of patients hospitalized with mechanical ventilation have respiratory distress syndrome, among which only 25% of cases have mild ARDS and the remaining 75% have moderate and severe symptoms.<sup>3</sup>

Until now, treatment of ARDS has focused on improving oxygenation through IMV, despite the high risk of causing ventilator-induced lung injury (VILI). This occurs when ventilatory parameters are not adequate for the patient, causing excessive transpulmonary pressures or significant modifications of pleural pressure that increase inflammation, alveolar damage and cause hemodynamic instability.<sup>2</sup>

Since 2009, in patients with severe ARDS in whom conventional mechanical ventilation has failed<sup>6,7</sup>, the use of venovenous extracorporeal membrane oxygenation has been proposed with the aim of mechanically assisting blood oxygenation and the elimination of carbon dioxide (CO<sub>2</sub>).<sup>1,5,7</sup> In ECMO-VV, extracorporeal gas exchange is governed by the same mechanism. From human physiology, the patient's volume is drained by the extracorporeal circuit to a centrifugal pump that in turn drives it towards an oxygenation membrane, generating a gas exchange without the need for lung participation. Thus, while the patient is on ECMO-VV ventilatory parameters can be decreased well below the usual requirements to maintain homeostasis and lung function, minimizing the damage induced by IMV, while maintaining organ function.<sup>8</sup>

The extracorporeal life support organization (ELSO) management guidelines recommend the use of ECMO-VV in patients with ARDS of any cause whose mortality risk is greater than 50%.<sup>9</sup> Although the efficacy of ECMO-VV is highly controversial, its use has increased markedly due to the good results obtained during the H1N1 influenza epidemic where survival values of 77% were achieved.<sup>10</sup> Some care centers recommend its early application when preventing and controlling VILI and, in addition, technological evolution and current designs have reduced the complexity of its use as well as the possible risks and adverse effects to be generated in the patient.<sup>5,11</sup>

In ECMO-VV oxygenation is determined by blood flow, hemoglobin concentration, hemoglobin saturation and oxygenator membrane properties. Decarboxylation depends on blood flow, gas sweep rate, incoming PaCO<sub>2</sub> and oxygenator membrane properties.<sup>12</sup> When using this device, the patient's arterial pH depends on the flow of gas in the oxygenator membrane, which at the start of the support is maintained in a 1:1 ratio with the flow of blood that is extracted to the circuit. Gas and blood flow are then regulated to keep PaCO<sub>2</sub> in an adequate range.<sup>13</sup>

In theory it is established that the blood flow entering the device in adult patients is 60 ml / kg / min to maintain a saturation of 85 to 90%. However, in ECMO-VV it is very common for a fraction of oxygenated blood to return to the oxygenator membrane reducing the effectiveness of the system, which is known as "recirculation". On the other hand, it should be considered that critical patients usually present anemia which would also influence the stipulated value of blood flow that must be extracted.<sup>12</sup> So there is no

Clear reference value that fits the state of severity of each patient, which is very important as it is closely related to the sweeping gas flow. It is also intended to clarify whether there is an alteration of PaO<sub>2</sub> or PaCO<sub>2</sub> this should be corrected by adjusting the parameters of ECMO or mechanical ventilator since usually, in a patient who does not use ECMO, when there is an alteration of arterial pH this is corrected by respiratory rate and / or the tidal volume of the ventilator.

Ventilation strategies in patients with ARDS have been studied in countless investigations and in 77% of the centers specialized in this technique they use the concept of "lung rest", which is a type of

protective ventilation with low tidal volume, low respiratory rate and high PEEP. However, it is still to be clarified how these parameters change as the transition from ECMO-VV to VMI takes place. There is also little literature regarding ECMO parameters such as blood flow, sweeping gas flow and oxygenator membrane; of which it has not been established how they should be modified as the functioning of the patient's native organs improves and he needs less extracorporeal support until the time of weaning.<sup>14</sup>

The objective of this study is to establish criteria for managing the parameters of mechanical ventilation and extracorporeal venous-venous membrane for the treatment of patients with ARDS, hoping in this way to provide a reference base in the adequate management of this pathology.

### **Materials and methods**

A systematic search of the PubMed electronic database of the National Center for Biotechnology Information, from March 29 to April 30, 2019, was conducted to collect articles reporting on the management of VMI and ECMO-VV parameters in the treatment of ARDS. For which two search strings composed of free, controlled and Boolean language were generated, the first string is focused on the parameters of the ECMO-VV while the second on the parameters of the VMI:

1. ((sweep gas flow) AND blood flow) AND (vv ecmo OR venovenous extracorporeal membrane oxygenation OR "extracorporeal membrane oxygenation"[MeSH]) AND (respiratory insufficiency OR respiratory failure OR ARDS OR "respiratory distress syndrome, adult"[MeSH]).
2. ((((((mechanical ventilation) AND invasive ventilation) AND "respiration, artificial"[MeSH]) AND (vv ecmo OR venovenous extracorporeal membrane oxygenation OR "extracorporeal membrane oxygenation"[MeSH])) AND (respiratory insufficiency OR respiratory failure OR ARDS OR "respiratory distress syndrome, adult"[MeSH]))

In the two searches, the date of publication of the articles was used as a filter, taking into account those that have been published for 10 years to the present, obtaining the most up-to-date information possible. In addition, no restrictions were applied based on language or place of publication. The citations were collected in a referral management software program called Zotero.

### ***Selection of studies***

Retrieved articles were included or rejected based on information obtained from the title, abstract or main text. Only studies that reported extensively on parameters of interest such as: 1) blood flow, 2) sweeping gas flow, 3) ECMO-VV and 4) ARDS were included in the first search chain. Studies containing information on: 1) tidal volume, 2) respiratory rate, 3) PEEP, 4) ECMO-VV and 5) ARDS were included in the second search chain. In both cases, articles containing information regarding arterial venous ECMO greater than 50% of the full text or whose study population were pediatric patients were eliminated.

### ***Data collection process***

Initially, we assessed the titles and abstracts of all retrieved citations according to the inclusion criteria. We screened full-text copies of studies when articles were considered to meet the inclusion criteria. The results were compared and those articles containing the required information were selected. The process followed the PRISMA guidelines for systematic reviews and meta-analyses.<sup>15</sup>

### ***Data extraction***

Table I and II summarized the descriptive data of each study, including title, objectives, author(s), and year of publication; technical information such as number of patients/animals studied, intubation, mode of mechanical ventilation, tidal volume (VC), positive end-expiratory pressure (PEEP), respiratory rate (RF), pH, ECMO mode, access route, size of cannula used, oxygenator membrane surface, sweeping gas flow, blood flow, CO<sub>2</sub> removal and duration of ECMO-VV.

## Results

### *Study selection and characteristics*

A total of 16 citations were identified in the first search and 42 in the second search, resulting in a total of 58 articles. Of these, 31 passed the first selection phase and full-text articles were retrieved. After secondary selection, 5 articles met the inclusion criteria and were included in the final analysis. 16–20 Figure 1 shows the PRISMA flowchart for inclusion and exclusion criteria.

Table I contains an overview of the included studies, all published after 2014. Two experimental studies<sup>16,17</sup>, two retrospective studies<sup>18,19</sup> and one case report were included<sup>20</sup>. Table II summarizes the included studies, describes the objectives, the subjects included, detailing their characteristics, the intervention performed and the results obtained. The experimental studies used a total of 16 pigs with induced ARDS<sup>16,17</sup>, one study includes 317 patients undergoing VV-ECMO with ARDS of different kinds that is not specified in detail in the article<sup>18</sup>, one study includes 7 patients with ARDS related to polytrauma<sup>19</sup> and a last study includes 1 patient with ARDS secondary to *Pneumocystis jirovecii* pneumonia<sup>20</sup>. All studies focused on the adult population, including experimental studies that were conducted on large animals, such as pigs that were kept in a certain environment so that the estimated CO<sub>2</sub> production was 200–280 ml / min which is comparable to an adult human at rest.

### *Methodological quality of included studies*

The methodological quality of the experimental studies<sup>(16,17)</sup> was evaluated with Study Quality Assessment Tools for before-after studies without a control group from the National Heart, Lung and Blood Institute,<sup>(21)</sup> resulting in a mean quality in both articles (63%). The retrospective studies and case studies were evaluated using the Newcastle-Ottawa scale<sup>22</sup> (Table III), one obtained 7 full stars of quality<sup>19</sup> which is equivalent to very good methodological quality, while the other articles obtained 6 stars<sup>18</sup> and 5 stars<sup>20</sup> with what is determined to be studies of medium methodological quality.

### *Synthesis of results*

The studies carried out in animals<sup>16,17</sup> used the right jugular vein as the route of cannulation, as for the studies done in humans, one of them <sup>18</sup> does not specify the cannulation site and the other two studies perform cannulation in the femoral vein, whether left or right<sup>19,20</sup>. The duration of ECMO-VV in one of the studies with pigs<sup>17</sup> is unknown, while in the other<sup>16</sup> the time of experimentation was one day, a situation that occurs similarly with respect to the number of days of use of IMV. The average duration of ECMO-VV in people was 8 days<sup>18–20</sup> and IMV ranged from 7 to 25 days<sup>19,20</sup>.

When a comparison was made between the SP of 0.8 m<sup>2</sup>, 1 m<sup>2</sup> and 1.3 m<sup>2</sup> with FS of 1000 ml / min in all cases, an increase of 11.8% in the efficiency of CO<sub>2</sub> removal between the first two types of SP; and with the third a slightly greater increase of 17.3%. Membrane surfaces of 0.8 m<sup>2</sup> or more were able to completely correct severe respiratory acidosis, provided that the FS rate is not less than 1000 ml / min, while smaller membrane lungs (0.4 m<sup>2</sup>) were not able to efficiently remove CO<sub>2</sub>, even if FS rates greater than 1000 ml / min were used, therefore, membrane lungs with a surface area of  $\geq$  0.8 m<sup>2</sup> could reduce the patient's initial PaCO<sub>2</sub> by up to 50 to 53% with FS rates of 1000 ml / min<sup>16,17</sup>.

The sweeping gas flow rate was clinically negligible when a small SP of 0.4 m<sup>2</sup> with FS rates less than 900 ml/min was used. The lung membrane with an SP of 0.8 m<sup>2</sup> and sweeping gas flow of 2 to 8 l/min showed results not very significant with FS rates of 300 to 600 ml / min, but when using FS values of 900 to 1800 ml / min, an increase in CO<sub>2</sub> removal was shown from  $55 \pm 9$  to  $70 \pm 14$  ml / min, with FS rates lower than these any increase in sweeping gas flow was inconsequential.<sup>16,17</sup>

In contrast one of the studies considers that the removal of CO<sub>2</sub> depends essentially on the type of ECMO system that is used and not on the flow of blood or gas flow, however, it states that blood flow

or sweeping gas flow can be increased to increase the removal of CO<sub>2</sub>. Thus, a blood flow of 1500 ml/min with a gas flow of 1.2 l/min allowed a CO<sub>2</sub> removal of 150 – 175 ml/min while with a blood flow of 4500 ml/min and sweeping gas flow of 2 l/min allowed a slightly higher CO<sub>2</sub> removal of 150 to 200 ml/min. Therefore, the ability to remove extra CO<sub>2</sub> bodily increases at high sweeping gas flow rates, as long as a membrane surface area of no less than 0.8 m<sup>2</sup> is employed with a blood flow greater than 900 ml / min.<sup>18</sup>

The transfer of oxygen according to Lehle<sup>18</sup> depends on the type of ECMO system ( $p = 0.002$ ), blood flow ( $p < 0.001$ ) and gas flow ( $p < 0.001$ ), with FS rates less than 3000 ml / min the transfer of oxygen was directly proportional to the FS, regardless of the gas flow rate used while at values higher than that it loses this relationship and begins to depend on the sweeping gas flow. A comparison made with three different membrane sizes to an FS of 1000 ml / min, it was observed that with said FS rate a maximum oxygen transfer 60 ml / min was achieved, showing that oxygen transfer is independent of SP and dependent on FS rate.<sup>16,17</sup>

One of the main advantages of ECMO-VV as it is already known is that it allows to apply a protective or ultraprotective ventilation strategy avoiding in this way barotrauma, volutrauma or oxygen toxicity.<sup>23</sup> In studies in pigs, they employ a protective strategy, in volume control mode with a VC of 220 - 250 ml, PEEP of 5 cmH<sub>2</sub>O and RF of 14 - 16 rpm.<sup>16,17</sup> The group of 7 patients were also ventilated with a protective strategy VC of 5.8 ml / kg of ideal weight (IQR: 4.3 to 7.2 ml / Kg), median PEEP 9.2 cmH<sub>2</sub>O (IQR: 8 to 10 cmH<sub>2</sub>O), median FiO<sub>2</sub> 0.4 (IQR: 0.3 to 0.4), median plateau pressure (Ppl) 21.8 cmH<sub>2</sub>O (IQR: 17.8 to 25.8 cmH<sub>2</sub>O).<sup>18</sup> In the case study they used parameters of ultraprotective ventilation, ventilation in pressure control mode, with maximum inspiratory pressure (PIP) of 15 cmH<sub>2</sub>O, PEEP 5 cmH<sub>2</sub>O, FR 10 rpm and FiO<sub>2</sub> 21%.<sup>20</sup>

The variation of these parameters occurred as the patient's health status improved, based on clinical signs such as pulmonary satisfaction, arterial oxygenation and chest x-ray.<sup>19</sup> The transition from ECMO-VV to VM began with the change of ventilation mode, from pressure control to pressure support, the RF rose from 10 to 25 rpm, the PIP was reduced from 15 to 11 cmH<sub>2</sub>O, the PEEP remained at very low values of 5 to 3 cmH<sub>2</sub>O, the VC was progressively increased from 200 to 370 ml in intervals of 100 to 200 ml and the FiO<sub>2</sub> was increased from 21% to 30%.<sup>20</sup> Roman in his study makes a comparison of the median pre and post ECMO-VV results where the VC step from 6.3 ml / kg ideal weight to 4.6 ml / kg ( $p = 0.01$ ), FiO<sub>2</sub> step from 1 to 0.4 ( $p = 0.007$ ), arterial pH rose from 7.29 to 7.43 ( $p = 0.01$ ), PaCO<sub>2</sub> decreased from 58 mmHg to 38 mmHg ( $p = 0.01$ ) and Ppl was not statistically significant, step from 26 cmH<sub>2</sub>O to 24.5 cmH<sub>2</sub>O ( $p = 0.07$ ).<sup>19</sup>

In the case study the weaning process started from the first day with the progressive decrease of the sweeping gas flow in ranges of 0.5 to 1.5 l / min from its initial value of 4 l / min until reaching zero.<sup>20</sup> Another of the studies followed the same procedure, gradually decreased the flow of gas until leaving the patient without this contribution, although it does not specify the values used, I also consider two groups of patients, those who are anticoagulated in which blood flow was reduced for a period of 2 - 3 hours, while, In patients without anticoagulation, the gas supply was gradually decreased while maintaining constant blood flow to avoid thrombotic complications during the process.<sup>19</sup>

## Discussion

This review includes studies conducted in animals and patients that combine the characteristics of ARDS with ECMO-VV, experimental articles conducted in animals are included as they play a key role in the investigation of ARDS, given the complexity of the pathophysiology and the scarce information in the field of ECMO-VV in adults.<sup>24</sup> All articles are very heterogeneous and although they provide information on the management of ECMO-VV together with the VMI, they show the wide variety of monitoring configurations that are currently used.

Initially blood flow and scavenging gas flow were considered as the main determinants in the CO<sub>2</sub> removal capacity of ECMO-VV, it has been determined from a more physiological point of view, which depends rather on a complex interaction of three factors: the area of the membrane surface of the lung, the blood flow rate and the sweeping gas flow rate.<sup>23</sup> The latter is significant only when an adequate blood flow rate (900 ml / min) is programmed together with a large membrane surface ( $\geq 0.8$  m<sup>2</sup>), although the greater the sweeping gas flow, the greater the CO<sub>2</sub> removal, this should not exceed 10 l / min, beyond that there is impaired oxygenation that must be avoided.<sup>25</sup>

The oxygenation transfer has been determined to be independent of the scavenging gas flow and the membrane surface, but not of the blood flow rate with which it maintains a directly proportional relationship, so a FS rate of 1000 ml / min is able to reach a maximum oxygen transfer 60 ml / min.<sup>16,17</sup> Although it is denied that there is a relationship between oxygen transfer and SP size, Lehle states that a lung membrane surface  $\geq 0.8$  m<sup>2</sup> ensures a greater oxygen transfer compared to a smaller one, a situation that happens in a similar way with the removal of CO<sub>2</sub>, so the need to always use large SP is reaffirmed.<sup>18</sup>

The mechanical ventilation parameters with which ECMO-VV is initiated differ greatly from one article to another, 60% use protective ventilation strategies and only 20% ultraprotective ventilation strategies. The modes controlled either by pressure or by volume seem the most used in this type of patients

when they are totally sedated and the functional alteration is too serious. In the studies carried out in pigs these were ventilated in volume control mode, probably due to the short duration of the experimentation (1 day) unlike the studies in patients which were ventilated in pressure control mode because in this way it is possible to have a daily control of the increase in VC as the patient improves, which would be the most advisable.

At the beginning of extracorporeal support VM parameters, such as PIP, PEEP and FiO<sub>2</sub> have been observed to be programmed as established by ELSO guidelines: PIP equal to or less than 35 mmHg, PEEP less than 10 cmH<sub>2</sub>O and FiO<sub>2</sub> equal to or less than 0.5.<sup>23,24,26</sup> All articles included regardless of the type of strategy remained within these ranges once ECMO-VV was established, except for RF which according to ELSO guidelines should be programmed in a range of 4-5 rpm to avoid mechanical stress of the lung,<sup>27</sup> however in the articles included the RF used varies between 10 to 16 rpm.<sup>16,17,20</sup> In contrast, a study conducted in 15 patients in European intensive care units uses an RF of 20 to 35 rpm,<sup>28</sup> which shows that RF should be initiated with high values that are related to the low tidal volumes established and can ensure the minute volume provided to the patient, therefore it would be advisable to perform an update around the RF scheduled at the beginning of extracorporeal support, that is based on the values currently used in clinical practice.

An attempt has been made to gather information to clarify the progression of the ventilator parameters until the moment of disconnection of the ECMO-VV support, however, the current studies are very little detailed in this regard, and the data found are contradictory so that it has not been possible to determine a standardized scheme of the progression of these, which can be attributed to the heterogeneity of ARDS and the different evolution between each patient. So this study is expected to initiate research and experimentation focused on a daily monitoring of IMV parameters in ECMO-VV.

Weaning of ECMO-VV will only be initiated once it has been proven that the patient's clinical signs are adequate and the contribution of sweeping gas flow

It is null without implying an alteration in gas exchange and hemodynamics. This is also confirmed by Torregrosa et al.<sup>23</sup> who establishes that in order to disconnect the ECMO-VV, the sweep gas flow

must be completely cancelled and that in these circumstances the ventilatory parameters must be adequate, i.e.  $FiO_2 \leq 0.5$ ,  $PIP \leq 35$  mmHg and  $PEEP \leq 10$  cmH<sub>2</sub>O.

The type of procedure that is carried out with the blood flow rate will depend on whether or not the patient is anticoagulated, if not, the blood flow will remain constant, otherwise it will progressively decrease in a period of 2 to 3 hours. In both cases, patients are observed for several hours, during which the ventilatory parameters necessary to maintain adequate oxygenation and ventilation without ECMO-VV are determined.<sup>19</sup> In this study the patient was anticoagulated despite that the blood flow remained constant, which indicates that the final procedure to be carried out will depend on the clinical picture of the patient and the experience and / or criteria of the treating physician.

### Conclusion

Oxygenation with ECMO-VV is an effective treatment alternative in the management of patients with ARDS that allows maintaining the necessary oxygenation and ventilation . A good elimination of CO<sub>2</sub> and greater oxygen supply will be achieved only when the triad of gas flow, blood flow and membrane surface is ideal, the wrong programming of any of these three aspects will affect the expected results of the treatment. It has not been possible to determine a standardized scheme of the progression of the parameters of mechanical ventilation, because each patient evolves differently and finally the heterogeneity of ARDS itself prevents determining a scheme in its treatment.

### Conflict of interest

The authors of this article declare that they do not present any conflict of interest.

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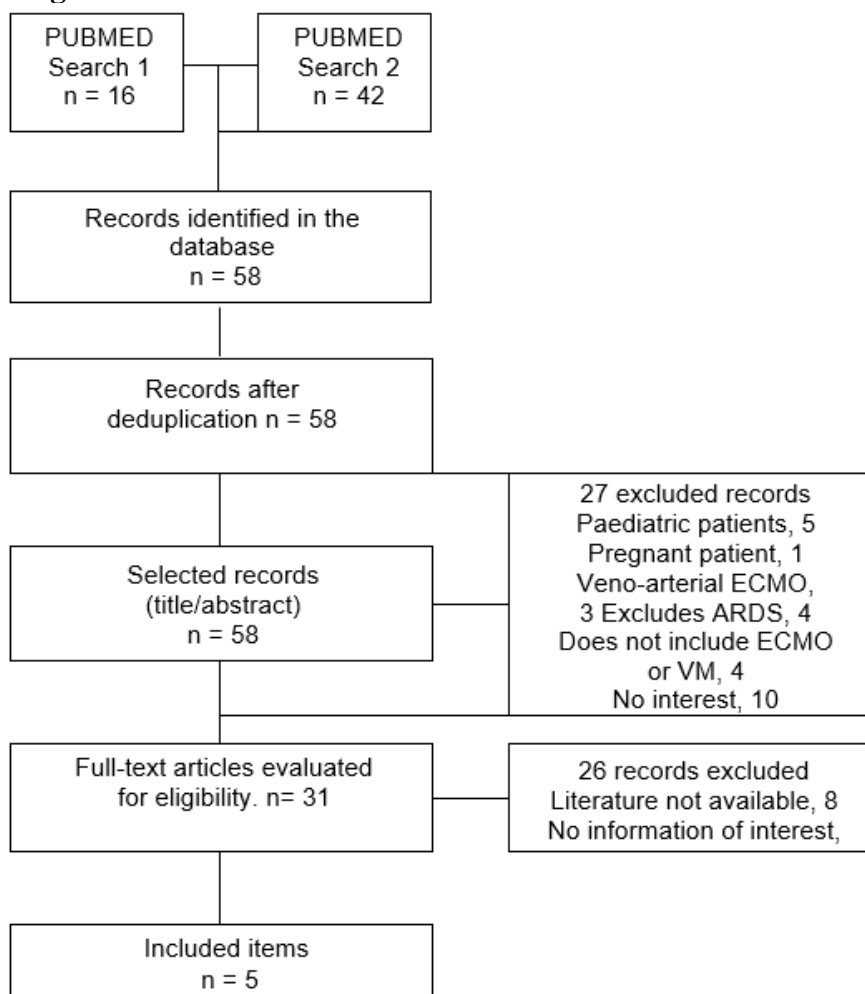
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**Figure 1.** PRISMA flowchart for inclusion and exclusion criteria.



**Table I.** Description of the studies included in the review.

I am a student	Year	Type of study	Species	Patients	Etiology ARDS	Cannulation	ECMO Duration (days)	VMI duration (days)
Karagiannidis(16)	2017	Experimental	Animal	7	Induced	VYD	1	1
Strassmann(17)	2019	Experimental	Animal	9	Induced	VYD	NE	NE
Lehle(18)	2014	Retrospective	Human	317	NE	NE	9±1	NE
Roman(19)	2015	Observational retrospective	Human	7	Polytrauma	VFD	9	25
Ali (20)	2016	Report of a case	Human	1	Pneumonia	VFI	6	7

NE - not specified; VYD - right jugular vein; VFD - right femoral vein; FIV - left femoral vein.

**Table II.** Summary of studies included in the review.

Author	Objective	Subject	Intervention
<b>Karagiannidis (16)</b>	Determine the optimal membrane SP area and technical requirements for ECMO-VV success.	7 pigs (body weight = $44.6 \pm 3.8$ kg) anesthetized, intubated with endotracheal tube (internal diameter, 7 mm) and ventilated (Servo-i) at 38 °C body temperature.	Use of four membrane lungs, with SP areas of 0.4, 0.8, 1.0 and 1.3 m <sup>2</sup> to perform ECMO-VV with FGB of 8 l / min, with each the FS was gradually increased from 250 to 1000 ml / min.
<b>Strassmann (17)</b>	Determine the impact of different FGB indices on CO <sub>2</sub> removal under different FS conditions and areas of SP.	9 pigs (body weight = $39 \pm 2$ kg) anesthetized, intubated with endotracheal tube (internal diameter, 7 mm) and ventilated with (Servo-i) with body temperature of 38 °C.	Using two SP lungs of 0.4 and 0.8 m <sup>2</sup> , in each the FS was gradually increased from 300 to 900 ml/min, with additional increases of up to 1800 ml/min with the larger SP. The FGB was titrated at each condition from 2 to 8 l/min in steps of 2 l / min.
<b>Lehle (18)</b>	Analyze the gas transfer capacity of different ECMO systems in clinical practice to support and guide Future application.	Retrospective study of data prospectively collected from 317 adults with severe respiratory failure requiring ECMO-VV support, since January 2009 until July 2013.	Analysis of the gas transfer capacity of four ECMO systems (PLS System, n = 163, CH Cardio Aid System, n = 59; Hilite 7000 LT HL System, n = 56; ECC.05 system, n = 39), the allocation was based on clinical availability.
<b>Roman (19)</b>	Describe the results of a new oxygenation membrane program extra corporeal in a Unit of intensive care.	Data from 22 patients requiring ECMO-VV from January 2011 to June 2014 were Collected from the medical history electronics.	Use of protective ventilation, VC = 6 – 7 ml / Kg theoretical weight, Ppl < 30 mmHg and PEEP was titrated after a recruitment maneuver. The patients with Pa/FiO <sub>2</sub> < 150 were incorporated into the Distress protocol and ventilation in prone position. Patients with refractory hypoxemia (Pa/FiO <sub>2</sub> < 100, FiO <sub>2</sub> > 0.6), respiratory acidosis pH < 7.2, and/or barotrauma after 12 - 24 h of strategies ventilatory, were evaluated for ECMO-VV.
<b>Ali (20)</b>	Presentation of a case of respiratory failure Potentially mortal Due to one infection grave by Pneumocystis Jirovecii Complicated by pneumomediastinum in one HIV-infected patient What Was Rescued by ECMO-VV.	A 26-year-old male has a dry cough, shortness of breath, pain in the 15-day chest, BMI 18.8 kg / m <sup>2</sup> , fever 38.9 °C, tachycardia (HR120 / min), tachypnea (FR 35 / min), hypoxia (pulse oximetry:85%) and normal blood pressure (126/76 mm Hg). The RX of thorax Showed Opacities Bilateral in Areas medium and lower.	Day 1 and 2, intermittent use of VIN. Day 4, the function respiratory impairment (RF 40/min; PaO <sub>2</sub> 50 mm Hg in FiO <sub>2</sub> 0.6), chest X-ray showed emphysema subcutaneous with pneumomediastinum and Infiltrated bilateral pulmonary. Intubates and starts VMs with VC 225 ml, PaO <sub>2</sub> /FiO <sub>2</sub> 200 mm Hg, FiO <sub>2</sub> 45% and PEEP 10 cmH <sub>2</sub> O. The patient has acidosis severe respiratory, PaCO <sub>2</sub> 109 mm Hg and pH 7.01. Her self place ECMO-VV, FS and FGB at 4 liters/min. The VM with ultra-protective strategy: PCV mode, PIP 15 cmH <sub>2</sub> O, PEEP 5 cmH <sub>2</sub> O, FR 10/min and FiO <sub>2</sub> 21%.

FGB - sweeping gas flow; FS - blood flow; SP - lung surface; FMO - multi-organ failure; X-ray - radiography; HR - heart rate; FR- respiratory rate; NIV - non-invasive mechanical ventilation; PCV - pressure-controlled ventilation; PSV - pressure support ventilation; VC - tidal volume; Ppl - plateau pressure; PEEP - positive end-expiratory pressure; PIP - positive inspiratory pressure.

**Table III.** Newcastle-Ottawa scale for included retrospective studies.

First author	Selection			Comparison		Results		Score
	Representativeness of the exposed cohort	Selection of the exposed cohort	Knowledge of the exhibition	Comparability of cohorts at the basis of design or analysis	Knowledge of the exhibition	It was the follow-up long enough for the result	Appropriateness of cohort follow-up	
<b>Lehle (18)</b>	★	--	★	★	★	★	★	6
<b>Roman (19)</b>	★	★	★	★	★	★	★	7
<b>Ali (20)</b>	--	★	★	--	★	★	★	5