ISSN 2715 - 6060
Padjadjaran Acute Care Nursing Journal Vol 2 No 2 April 2021

Review

Management of Acute Respiratory Distress Syndrome (ARDS) patients: A Literature Review

Etika Emaliyawati[1], Hamidah Nurhalimah[2], Hesty Adha[2], Inas Shintia Balqis[2], Ismailah Alam[2], Michael Mochamad Danny[2], Novarina Ismayani Anumilah[2], Rahdatul Aisyiyah[2]
[1]Department of Emergency and Critical Care, Faculty of Nursing, Universitas Padjadjaran
[2]Undergraduate Students, Faculty of Nursing, Universitas Padjadjaran

ARTICLE INFO
Article history:
Received 03-06-2021
Received in revised from 05-07-2021
Accepted 06-07-2021

Keyword:
Acute Respiratory Distress Syndrome, treatment, management

Other information:
Email of Author:
etika@unpad.ac.id
Corresponding Author:
Etika Emaliyawati

ABSTRACT
In general, Acute Respiratory Distress Syndrome or ARDS is acknowledged to be the cause of 10% opatients requiring ICU care, and about 3 million patients worldwide experience it. Despite the data, up to these days there haven't been many treatments that are considered to be effective in preventing or treating ARDS.
This research is a literature review with a narrative approach in which the researchers analyze several research articles. The present study aims to analyze the management of ARDS in reducing mortality, improving lung function and airway effectiveness. The articles were searched based on the publication year 2016-2020, with the keywords "Acute Respiratory Distress Syndrome" AND "Oxygen Saturation", "Acute Respiratory Distress Syndrome" AND "Treatment", "Acute Respiratory Distress Syndrome" AND "Management"; as well as the databases of PubMed, EBSCO and American Journal of Clinical Pathology.
Based on the 14 articles selected using inclusion criteria, it was found that there were 8 treatments given to the ARDS patients to reduce mortality, namely Non-Invasive Ventilation (NIV), the use of corticosteroids, UC-MSC (umbilical cord mesenchymal stem cells), oxygen therapy, mechanical ventilation, HFNC, prone position, open lung approach (OLA), and simvastatin.
Of the 8 analyzed treatments, 3 interventions were found to have the highest significance of improvement in lung function and quality improvement in several indicators such as decreased mortality rate, increased saturation, decreased hospitalization time, etc. These interventions were: (1) Non-Invasive Ventilation (p value <0.001); (2) simvastatin (p value <0.001); (3) Corticosteroid (methylprednisolone) (p value <0.001).

Introduction

Acute Respiratory Distress Syndrome (ARDS) has reached 200,000 cases each year in the United States and is the cause of 75,000 death cases. In general, ARDS is acknowledged to be the cause of the 10% patients requiring ICU care, and about 3 million patients worldwide experience it. As many as 24% of ARDS patients in the world are treated with a mechanical ventilator in the ICU (Fan, Brodie, & Slutsky, 2018). The mortality rate for ARDS patients who are treated in ICU hospitals in Indonesia reaches more or less 40% (Aboet & Maskoen, 2018).

ARDS is a state of acute lung injury that occurs due to the inflammation in the lungs which increase the pulmonary vascular permeability and make the lungs lose air containing oxygen (Aboet & Maskoen, 2018). The predisposing and risks factors for ARDS are shock, aspiration, aortic surgery, emergency surgery, heart surgery, acute abdomen, head trauma, pneumonia, obesity BMI> 30, diabetes, hypoalbuminemia, FIO2> 0.35, pH <7.35 and tachypnea (Walkey, Summer, Ho, & Alkana, 2012).

The definition of ARDS was first put forward by Asbaugh at al (1967) as severe hypoxemia with an acute onset. ARDS is a life-threatening condition caused by the inflammation occurred in the lung parenchyma resulting in hypoxemia, impaired gas exchange and organ failure (Lee, J, & M, 2011). According to the America-Europa Consensus Conference Committee, it is characterized by a PAWP (pulmonary artery wedge pressure) factor <18. Judging from the PaO2: FiO2 ratio, ARDS can be categorized into severe criteria (PaO2: FiO2 ratio <100), moderate criteria (PaO2: FiO2 ratio 100-200) and light criteria (PaO2: FiO2 200-300 ratio) (Marco, R, & T, 2012).

The mortality rate caused by ARDS is proportional to the severity rate, namely mild ARDS 27%, moderate ARDS 32%, and severe ARDS 45% (Diamond, Hector L, Sanghavi, Sidhart, & Mahapatra, 2021). In ARDS cases triggered by COVID-19 pneumonia alone, the mortality rate reaches 50-94%. According to Fatoni & Rakhmatullah, (2021), up to November 2020, the data on the COVID-19 cases at Intensive Care Unit (ICU) of Dr. Saiful Anwar Hospital, Malang and Karsa Husada Batu Hospital indicated that the mortality rate reached 47% to 81.7%.

According to the research done by Kusuma et.al, (2015), there are several predictive factors for the death in the ARDS patients in the ICU. Among others are pneumonia, COPD, leukocyte count, MODS, and the use of vasopressors. Moreover, there are some other studies which show that the APACHE score, the use of mechanical ventilators, hypoalbuminemia, and acidosis can become the factors that influence the mortality rate of ARDS patients.

Up to these days, treatments that are proven to be effective in preventing or treating ARDS are still few. The main treatment strategy is supportive care which focuses on reducing the shunt fraction, increasing oxygen supply, reducing oxygen consumption, and avoiding further injury. A pulmonary protective ventilation strategy is suggested to reduce the lung injury. Mild-moderate ARDS patients can benefit from non-invasive ventilation to avoid endotracheal intubation and invasive mechanical ventilation. Extracorporeal membrane oxygenation (ECMO) has recently been recommended as a rescue therapy in refractory hypoxemic ARDS (Diamond et al., 2021).

Considering the importance of ARDS management to reduce the mortality rate due to the respiratory failure that occurs, the authors are interested in conducting a literature review related to the management or treatments given to the ARDS patients.

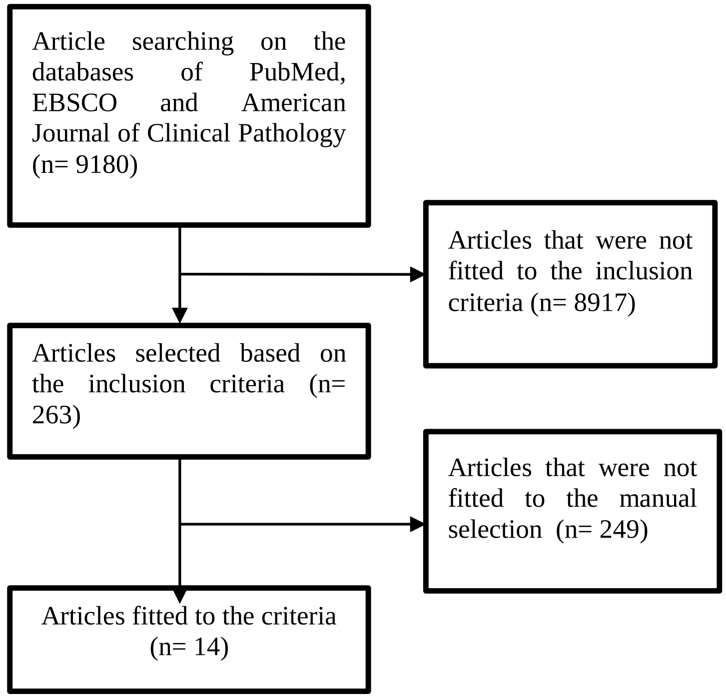
Method

This research is a literature review with a narrative approach in which the authors analyzed several research articles. The purpose of this study was to analyze the effective management of Acute Respiratory Distress Syndrome or ARDS. To achieve this objective, the first step taken was to identify the clinical information related to ARDS using the PICO method (P = Patient, Population, Problem; I = Intervention; C = Comparison, Control; O = Outcome). In this study, the PICO arrangement was; P = patients with ARDS; I = management / treatment to handle ARDS; and O = decreased mortality, improved lung function, and effectiveness of the airway. For 'C', the author did not specify it.

Results

The articles were searched in the online databases, particularly PubMed, EBSCO and the American Journal of Clinical Pathology. The keywords used during the searching process were; “Acute Respiratory Distress Syndrome” AND “Oxygen Saturation”, “Acute Respiratory Distress Syndrome” AND “Treatment”, “Acute Respiratory Distress Syndrome” AND “Management”. In the initial stage, the researchers obtained 9180 articles from PubMed, EBSCO and American Journal of Clinical Pathology databases. In the second stage, the researchers underwent the articles screening using the inclusion criteria, namely RCT research designs published in English and within the year of 2016-2021. From that process, the articles obtained were 263 articles. Then in the final stage, the researchers manually selected the articles by taking into account the content of the articles and its relevance to the topics discussed. In the end, the authors chose 14 articles which were later analyzed and discussed.

Figure 1. Article Filtering Process



Discussion

This literature review showed that there are 8 treatments used in ARDS patients to reduce mortality rate, namely Non-Invasive Ventilation (NIV), the use of corticosteroids, UC-MSC (umbilical cord mesenchymal stem cells), oxygen therapy, mechanical ventilation, HFNC, prone position, open lung approach (OLA), and simvastatin.

1. Non-Invasive Ventilation

The management of ARDS requires a systematic and intensive approach that reduces the risk of secondary injuries on the lung and other organs. One of the management measures for ARDS is the use of ventilation. In patients with ARDS, face mask ventilation is considered to be unhelpful. A higher positive end-expiratory pressure (PEEP) level is often required to increase oxygenation. However, at a high PEEP, face mask intolerance and air leakage can hinder effective oxygenation. Therefore, face masks have limitations that can contribute to the decrease of the effectiveness during an Acute Hypoxemic Respiratory Failure. An alternative to this is to use a Non-Invasive Ventilation (NIV) delivered by a helmet, a transparent object covering the entire patient's head with a soft collar neck seal. This interface helmet provides several advantages over face masks such as increased reliability and less air leakage due to the less contact between the helmet and face, as well as the integrity of the neck seal. Therefore, the helmet medium allows the titration of positive airway pressure to be increased without significant air leakage. This could reduce intubation and prolong the benefits of NIV for more ARDS patients.

Research conducted by Patel et al., (2016) indicated that NIV delivered by a helmet can increase the rate of endotracheal intubation rate among patients with ARDS (39 NIV via face mask and 44 NIV via helmet) at the ICU of the University of Chicago, America. The study used a randomized control trial method with the outcome criteria using RR instruments, oxygen saturation, FiO2, PEEP, Acute Physiology and Chronic Health Evaluation (APACHE) II and Hazard ratios (HRs). The results showed that the intubation rate was 61.5% (n = 24) for the mask group and 18.2% (n = 8) for the helmet group (absolute difference, −43.3%; 95% CI, −62.4% to −24.3%; P <0.001). The number of ventilator-free days was significantly higher in the helmet group (28 vs 12.5, P <0.001). In 90 days, there were only 15 patients (34.1%) in the helmet group who passed away compared to those of in the face mask group which were 22 patients (56.4%) (Absolute difference, −22.3%; 95% CI, −43.3 to −1.4; P = 0.02). A helmet NIV significantly reduces the intubation and mortality rates of ARDS patients. The PEEP effect and oxygen flow of the helmet NIV can increase oxygen and respiratory system.

2. Corticosteroids

The results of Baek's et al., (2021) study showed that the corticosteroid intervention group (59.2%) was significantly higher than the control group (48.4%) with a value (p = 0.021). In the corticosteroids group, the drug used is methylprednisolone at a dose of 40-180 mg / day. This corticosteroid therapy can be used in the initial phase of moderate to severe ARDS. It can increase survival for 28 days (odds ratio 1.031; 95% confidence interval, 0.657-1.618) with p values = 0.895 and for 90 days (odds ratio, 1.435; 95% confidence. interval, 0.877-2.348) with a value of p = 0.151.

Another result of the analysis showed that the treatment that can be given to the ARDS patients with COVID-19 was by giving dexamethasone. The use of dexamethason can increase the number of ventilator-free days of the patients with ARDS with standard or intravenous plus care. There was a difference between standard care and intravenous plus. Standard care was much more significant than intravenous plus in a way that it could significantly increase the number of ventilator-free days (days without mechanical ventilation) which was about 28 days. 20 mg of dexamethasone can be administered intravenously to the patients with COVID-19 ARDS once a day for 5 days, followed by 10 mg once a day for an additional 5 days or until the patients get discharged from the ICU (Tomazini et al., 2020).

Another meta analysis covering four RCT articles also showed that in the corticosteroid group, out of 385 patients, 108 (28.1%) passed away, while in the control group, 139 out of 357 patients (38.9%) died (combined OR, 0.61; 95% confidence interval, 0.44 - 0.85). All these findings referred to the cause of the death in the 28 or 30 day periods. Meanwhile, for the cause of death at 60 days, the three RCTs showed different results. In the corticosteroid group, 78 of 300 patients (26%) died, while in the control group, 101 of 265 patients (38.1%) died (Combined OR, 0.57; 95% CI, 0.40 - 0.83). The secondary results showed that corticosteroid treatment significantly prolonged ventilator-free days (4 RCTs: mean difference, 3.74; 95% CI, 1.53 - 5.95), but caused hyperglycaemia (3 RCTs: pooled OR, 1.52; 95% CI, 1.04 - 2.21). Therefore, ARDS patients who were given corticosteroid treatment experienced significant increase in short-term survival (Hirano et al., 2020).

Research conducted by Villar et al.,(2020) showed that ARDS patients given dexamethasone experienced a decrease in Sepsis-Related Organ Failure Assessment (SOFA) scores in the third day after starting the treatment, and an increase in PaO2 / FiO2 on the sixth day compared to the control group. The average number of extrapulmonary organ failures varied between the intervention and control groups. The side effects of the treatment were hyperglycemia (blood glucose> 180 mg / dL) and new infections (such as pneumonia or sepsis). The occurrence of hyperglycemia in the first 10 days after randomization was the same between the two groups. Dexamethasone did not increase the type and frequency of the infectious complications when the patients were in the ICU. However, early dexamethasone administration can reduce the duration of mechanical ventilation and the death cases in patients with moderate to severe ARDS.

The results of the study done by Meduri et al., (2016) showed that for 28 days there was a difference in the mortality rate of the placebo group and the methylprednisolone group before being given Unassisted Breathing (UAB) (12% vs 29%; p <0.001) and after UAB of (80% vs 50%; p <0.001). In the methylprednisolone group, the UAB administration time was shorter (p <0.001) and the hospital mortality rate was lower than the placebo group (20% vs 33%; p value 0.006). Moreover, the mechanical ventilator use and the ICU stay were higher and longer in the placebo group than in the methylprednisolone group (p <0.001). In the 14 days before the onset of ARDS, there was a decrease in the mortality rate in the hospital, namely 36% vs 49% (p value = 0.035). The use of methylprednisolone can increase the resolution of ARDS which results in an increase in the broad spectrum and a decrease in both mortality and hospitalization time.

3. UC-MSC

The research carried out by Lanzoni et al., (2021) showed the effect of umbilical cord mesenchymal stem cells (UC-MSC) on the patients with Covid-19 ARDS. In this study, the intervention group experienced a significant increase in survival by 91% which was higher than the control group (42%) (p = 0.015), in SAE-free survival (p = 0.008) and in recovery (p = 0.3). The intervention group that was given UC-MSC infusion in 50 ml containing serum albumin and heparin did not experience any bad side effects. In fact, on the sixth day, the group experienced a significant decrease in the inflammation of cytokines. The UC-MSC infusion is safe and gives benefits to the patients with COVID-19 ARDS.

4. Simvastatin

The prevention of the severity and progression of ARDS can be done by administering anti-inflammatory drugs in accordance with the pathophysiology of ARDS. ARDS is a cause of respiratory failure in critically ill patients. Previous studies which focused on ARDS and obtained the data from randomized controlled trials in the US have identified two distinct sub-phenotypes with different responses to mechanical ventilation and fluid therapy. More research are needed to determine whether these subphenotypes can be identified in the non-US patient population using different data sets, and more importantly whether these subphenotypes respond differently to the given pharmacotherapy. Simvastatin has the benefit of increasing survival rates in ARDS patients with subphenotypes that arise from hyperinflammatory ARDS. Simvastatin, a type of HMG CoA reductase inhibitor, not only has function to lower cholesterol levels (anti-cholesterolemia) but also has an anti-inflammatory effect on the lungs and an immunomodulating effect on endothelial function. Based on its important effects, simvastatin may be able to improve clinical outcomes in handling inflammation and infection in the ARDS patients.

The study of Calfee et al., (2018), investigated the symptoms of ARDS subphenotype and the patients' responses to the pharmacotherapy effect of simvastatin. The study involved 539 non-US patients drawn from 40 general ICUs in UK and Ireland, and used a random control trial method with the measuring criteria, the Interleukin and Soluble tumor necrosis factor receptor 1 (sTNFr1). The results showed that there were two sub-phenotypes; the first one was the hypoinflamated sub-phenotype given to 353 (65%) patients and obtained a value (p <0.0001), and the second was the hyperinflammatory subphenotype given to 186 (35%) patients. The clinical and biological characteristics of the two subphenotypes were similar to those of previous studies. Compared to those of with hypoinflammatory subphenotype, patients with the hyperinflammatory subphenotype had fewer ventilator-free days (median 2 days [IQR 0-17] vs. 18 [IQR 0–23]; p <0 · 0001), fewer non-pulmonary organ failure-free days (15 [0 -25] vs. 27 [21–28]; p <0 0001), and higher 28-day mortality (73 [39%] vs. 59 [17%]; p <0 0001). Although there was no difference in 28-day survival between the placebo and simvastatin patients in HARP-2, a significantly different survival was identified in patients categorized by treatment and subphenotype (p <0.0001). Specifically, in the hyperinflammatory subphenotype group, the patients treated with simvastatin had a significantly higher 28-day survival than those given placebo (p = 0.008).

5. Oxygen Therapy

In ARDS patients, the National Heart Lung and Blood Institute ARDS Clinical Trials Network recommends a target partial pressure of arterial oxigen (PaO2 between 55 and 80 mmHg). The prospective validation for this range in patients with ARDS is still limited. The research conducted by Barrot et al., (2020) found several findings including death from any cause at 28 days after randomization to the patients, death in the ICU at day 90, sequential organ failure assessment scores which were calculated without a respiratory component on day 0, 3 and 7, as well as ventilator-related pneumonia and septicemia for the first 28 days. The other outcomes found were cardio-vascular complications, a new-onset arrhythmias or cardiac ischemic events, and vasopressor use which was recorded during the first 7 days.

The study conducted by Barrot et al., (2020) aimed to determine whether oxygen conservatism would reduce mortality rate of the ARDS patients at 28 days compared to the regular liberal oxygen. The study was conducted using the Randomized Controlled Trial method in 13 ICUs in France from June 2016 to September 2018. The patients who were selected as the participants were those who have been intubated and have received mechanical ventilation for less than 12 hours for ARDS, a PaO_2: FiO_2 ratio of 300 mmHg or less. The exclusion criteria were long-term use of oxygen therapy or noninvasive ventilation at home, heart attack, traumatic brain injury and cranial hypertension as the reason of hospitalization in the ICU. If the patients were unable to write the informed consent, the information would be given to the patient's immediate family and included to the emergency consent procedure.

By using both inclusion and exclusion criteria, 205 ARDS patients were obtained. The total participants were then randomly assigned to the liberal oxygen group (103 people) and the conservative oxygen group (102 people). The randomization was stratified by age (<45 years, 45-65 years,> 65 years), and the severity of respiratory failure which was evaluated according to PaO_2: FiO_2 (less than 150 mmHg or> 150 mmHg), with PEEP of 5 cm water and FiO_2 60 -100%. The patients were assigned to the liberal oxygen group (target PaO_2 between 90-105 mmHg) and the conservative oxygen group (target PaO_2 between 55-70 mmHg) for the first 7 days with the invasive mechanical ventilation or until the extubation (if extubation was performed earlier).

In regard to the arterial blood gas level, SpO_2 was maintained at a level of at least 96% in the liberal oxygen group and 88-92% in the conservative oxygen group. If the PaO_2 was not within the predetermined range, FiO_2 would be modified by 0.05 (absolute value) if the difference from the target was less than 5 mmHg and by 0.10 if the difference was greater. When the arterial gas levels were measured, the pulse oximetry was compared with the arterial oxygen saturation (SaO_2) in order to adapt to SpO_2 monitoring. During the 6 hour interval of the measurement, fiO_2 was modified by 0.05 (absolute value) every 5 minutes until the desired SpO_2 was reached.

6. Mechanical Ventilation

Obese patients are more susceptible to alveolar derangement. This happens as a consequence of heavy chest wall and an increase in intra-abdominal pressure, a characteristic that results in decreased respiratory system compliance and low lung volume breathing. Therefore, obese patients with ARDS would benefit from higher PEEP to counteract this impact. However, additional PEEP in nonobese ARDS patients can lead to an increase in VILI caused by the excess distention from the normal alveoli (Bime et al., 2016).

From the analysis conducted by Bime et al (2016), it was found that in obese ARDS patients, a high PEEP ventilation strategy contributed to the reduction of 60-day hospital mortality. The effect of the PEEP strategy on the rate of barotrauma or the patients' proportion achieving unaided breathing on day 28 did not differ in terms of the obesity status. The benefits of the PEEP strategy that the obese patients can get can be outweighted by the potential harms that the strategy has for the non-obese patients.

A high PEEP strategy can be dangerous in non-obese patients, given that severe VILI can manifest clinically in the form of barotrauma. Barotrauma during the use of mechanical ventilation in ARDS patients is believed to be caused by excess distension and subsequent injury to previously normal parts of the lung, or by the repetitive opening and closing of the lung electasis section.

In another study, the Open Lung Approach (OLA) could be safely applied to the patients with ARDS. The OLA and ARDSnet protocols are the use of lung recruitment and PEEP reduction trials versus the ARDSnet table to administer FiO_2 and PEEP. This study demonstrated the safety of applying OLA to treat the patients with ARDS. The side effect rates for OLA and ARDSnet were shown to be low.

Although the hemodynamic side effects and transient hypoxemia may surface, these problems can be treated with fluids following the ARDS protocol. OLA significantly increased oxygenation, lung mechanics and driving pressure. Moreover, the approach did not affect the duration of ventilation and ICU support as well as 60-day mortality in patients with ARDS.

7. HFNC

Humidified high-flow nasal cannula (HFNC) requires less intensive nursing care and can be given in a common ward area. If the use of HFNC can reduce the proportion of patients requiring invasive positive pressure ventilation or NIV in the emergency department, then there are also potential benefits of it related to a reduction of the harms to the patients, a decrease in resource use, a shorter hospital stay time, and an increase in the availability of high dependency beds in the hospitals (Jones et al., 2016).

However, according to Jones's et al., (2016) study, compared to the standard oxygen therapy, HFNC could not reduce the need of the ARDS patients for NIV or invasive mechanical ventilation. In addition, there was no difference in the length of stay (LOS) in the emergency department in the two groups. One participant in the standard oxygen group experienced apnea, and seven participants had decreased GCS scores, the three of which were believed to be caused by acute hypercapnia. There were no clinical side effects associated with the use of HFNC. Post-hoc analysis showed that HFNC reduced the need for increased oxygen therapy within the first 24 hours of admission

The results of the research done by Thille et al (2019) indicated that out of 648 patients, there were 641 patients who successfully finished the experiment. The average extubation time was at day 7 with a proportion of 11.8% for HF nasal canules with NIV and 18.2% for HF nasal canules without NIV. There were several different findings obtained in the study. The first one was respiratory failure after extubation on day 7 by 21% for nasal cannula HF with NIV, and 29% for nasal cannula HF without NIV (p value = 0.02). The second one was re-insertion of ventilator (reintubation) after the patients were discharged from the ICU by 12% on the HF nasal cannula with NIV and 20% on the HF nasal cannula without NIV (p value = 0.009. Third, the ICU mortality rate was not significant in both groups; in the nasal HF group cannula with NIV was 6% and HF nasal cannula without NIV was 9% (p value = 0.25). The use of HF nasal oxygen cannula with NIV after extubation can significantly reduce the risk of respiratory failure at the time of extubation.

8. Prone Position

The survival rate of the severe ARDS patients in the prone position intervention group was higher than that of in the supine position intervention group. Despite the fact, mortality in the supine group was shown to be lower. This finding may be influenced by the category of the patients such as the patients with severe ARDS who were selected based on PEEP and FiO2 levels, and the patients who were selected within a period of 12-24 hours after ARDS.

The prone position is recommended for ARDS patients to relieve severe hypoxemia and prevent lung injury. This result is in line with the previous studies showing that the prone position, compared to the supine position, significantly reduces overinflated lung areas and promotes alveolar recruitment. The reduction in excess distention and the increase in alveolar recruitment can help prevent ventilator-induced lung injury by equalizing the distribution of stress and tension within the lungs (Guerin et al, 2019).

The roles of the nurse

The role of the critical nurses is to provide direct and intensive care to patients who are in a critical or life-threatening condition. Critical nurses are able to quickly deal with patients in emergency situations by providing nursing services (care givers). The nurses are also able to use specific equipment in the intensive room, become leaders and collaborators with other health teams and patient families, and provide education to the patients and families regarding the care given (educators). The critical nurses are able to be mediators or facilitators between patients, families and other health teams, respect the patients' rights and values, support and respect the patients' autonomy, and communicate the hopes and desires of patients and families (advocators) (Uveges, Milliken, & Alfred, 2019).

Conclusions

The present literature review found that there are several treatments that can be used in ARDS patients to reduce mortality, namely Non-Invasive Ventilation (NIV), use of corticosteroids, UC-MSC (umbilical cord mesenchymal stem cells), oxygen therapy, mechanical ventilation, HFNC, prone position, open lung approach (OLA), and simvastatin. Out of 8 interventions that have been analyzed, three interventions are considered to have the highest significance in lung function improvement, and quality improvement in several indicators such as decreased mortality, increased saturation, decreased hospitalization time, etc. The three interventions are: (1) Non-Invasive Ventilation (p value <0.001) (Patel et al., 2016); (2) Use of simvastatin (p value <0.001) (Calfee et al., 2018); (3) Administration of corticosteroids (methylprednisolone) (p value < 0.001) (Meduri et al., 2016). To achieve the maximum benefits, these should be carried out and adjusted to the needs and conditions experienced by the patients.

It is expected that the hospitals improve the quality of care for ARDS patients by applying several treatments that have been proven to be effective in the previous studies.

It is expected that there are further research which focus on investigating the effectiveness of the treatments on reducing the mortality in the characteristics of ARDS patients in Indonesia**.**

References

Aboet, A. A., & Maskoen, T. T. (2018). Acute Respiratory Distress Syndrome (ARDS). *Anesthesia & Critical Care*, *36*(2), 57–63.

Baek, M. S., Lee, Y., Hong, S. B., Lim, C. M., Koh, Y., & Huh, J. W. (2021). Effect of corticosteroid therapy in the early phase of acute respiratory distress syndrome: A propensity-matched cohort study. *Korean Journal of Internal Medicine*, *36*(1), 145–153. https://doi.org/10.3904/kjim.2019.153

Barrot, L., Asfar, P., Mauny, F., Winiszewski, H., Montini, F., Badie, J., … Capellier, G. (2020). Liberal or Conservative Oxygen Therapy for Acute Respiratory Distress Syndrome. *New England Journal of Medicine*, *382*(11), 999–1008. https://doi.org/10.1056/nejmoa1916431

Bime, C., Fiero, M., Lu, Z., Oren, E., Berry, C. E., Parthasarathy, S., & Garcia, J. G. N. (2016). High Positive End Expiratory Pressure is Associated with Improved Survival in Obese Patients with Acute Respiratory Distress Syndrome. *Physiology & Behavior*, *176*(1), 100–106. https://doi.org/10.1016/j.amjmed.2016.09.029.High

Calfee, C. S., Delucchi, K. L., Sinha, P., Matthay, M. A., Hackett, J., Shankar-Hari, M., … Sellors, G. (2018). Acute respiratory distress syndrome subphenotypes and differential response to simvastatin: secondary analysis of a randomised controlled trial. *The Lancet Respiratory Medicine*, *6*(9), 691–698. https://doi.org/10.1016/S2213-2600(18)30177-2

Diamond, M., Hector L, P. F., Sanghavi, D., Sidhart, & Mahapatra. (2021). Acute Respiratory Distress Syndrome.

Fan, Brodie, & Slutsky. (2018). Acute respiratory distress syndrome advances in diagnosis and treatment. *JAMA - J Am Med Associat*, *319*(7), 698–710.

Fatoni, A. Z., & Rakhmatullah, R. (2021). Acute Respiratory Distress Syndrome (ARDS) pada Pneumonia COVID-19. *Journal of Anaesthesia and Pain*, *2*(1), 11–24. https://doi.org/10.21776/ub.jap.2021.002.01.02

Guérin, C., Reignier, J., Richard, J.-C., Beuret, P., Gacouin, A., Boulain, T., … Ayzac, L. (2019). Prone Positioning in Severe Acute Respiratory Distress Syndrome. *New England Journal of Medicine*, *368*(23), 2159–2168. https://doi.org/10.1056/nejmoa1214103

Hirano, Y., Madokoro, S., Kondo, Y., Okamoto, K., & Tanaka, H. (2020). Corticosteroid treatment for early acute respiratory distress syndrome: a systematic review and meta-analysis of randomized trials. *Journal of Intensive Care*, *8*(1), 1–8. https://doi.org/10.1186/s40560-020-00510-y

Jones, P. G., Kamona, S., Doran, O., Sawtell, F., & Wilsher, M. (2016). Randomized controlled trial of humidified high-flow nasal oxygen for acute respiratory distress in the emergency department: The HOT-ER study. *Respiratory Care*, *61*(3), 291–299. https://doi.org/10.4187/respcare.04252

Kacmarek, R. M., Villar, J., Sulemanji, D., Montiel, R., Ferrando, C., Blanco, J., … Suárez-Sipmann, F. (2016). Open lung approach for the acute respiratory distress syndrome: A pilot, randomized controlled trial. *Critical Care Medicine*, *44*(1), 32–42. https://doi.org/10.1097/CCM.0000000000001383

Kusuma, I. F., Trisnawati, I., & Budiono, E. (2015). Faktor-Faktor yang mempengaruhi mortalitas pasien acute respiratory distress syndrome di ICU. *Indo Journal Chest Critical and Emergency Medical*, *2*(3), 103–106.

Lanzoni, G., Linetsky, E., Correa, D., Messinger Cayetano, S., Alvarez, R. A., Kouroupis, D., … Ricordi, C. (2021). Umbilical cord mesenchymal stem cells for COVID-19 acute respiratory distress syndrome: A double-blind, phase 1/2a, randomized controlled trial. *Stem Cells Translational Medicine*. https://doi.org/10.1002/sctm.20-0472

Lee, K., J, K., & M, P. (2011). Acute respiratory distress syndrome caused by miliary tuberculosis: a multicentre survey in South Korea. *INT J TUBERC LUNG DIS*, *15*(8), 1099–1103.

Marco, R., R, G., & T, T. (2012). Acute respiratory distress syndrome: The Berlin definition. *JAMA - Journal of the American Medical Association*, *307*(23), 2526–2533.

Meduri, G. U., Bridges, L., Shih, M. C., Marik, P. E., Siemieniuk, R. A. C., & Kocak, M. (2016). Prolonged glucocorticoid treatment is associated with improved ARDS outcomes: analysis of individual patients' data from four randomized trials and trial-level meta-analysis of the updated literature. *Intensive Care Medicine*, *42*(5), 829–840. https://doi.org/10.1007/s00134-015-4095-4

Patel, B. K., Wolfe, K. S., Pohlman, A. S., Hall, J. B., & Kress, J. P. (2016). Effect of noninvasive ventilation delivered by helmet vs face mask on the rate of endotracheal intubation in patients with acute respiratory distress syndrome a randomized clinical trial. *JAMA - Journal of the American Medical Association*, *315*(22), 2435–2441. https://doi.org/10.1001/jama.2016.6338

Thille, A. W., Muller, G., Gacouin, A., Coudroy, R., Decavèle, M., Sonneville, R., … Frat, J. P. (2019). Effect of Postextubation High-Flow Nasal Oxygen with Noninvasive Ventilation vs High-Flow Nasal Oxygen Alone on Reintubation among Patients at High Risk of Extubation Failure: A Randomized Clinical Trial. *JAMA - Journal of the American Medical Association*, *322*(15), 1465–1475. https://doi.org/10.1001/jama.2019.14901

Tomazini, B. M., Maia, I. S., Cavalcanti, A. B., Berwanger, O., Rosa, R. G., Veiga, V. C., … Azevedo, L. C. P. (2020). Effect of Dexamethasone on Days Alive and Ventilator-Free in Patients with Moderate or Severe Acute Respiratory Distress Syndrome and COVID-19: The CoDEX Randomized Clinical Trial. *JAMA - Journal of the American Medical Association*, *324*(13), 1307–1316. https://doi.org/10.1001/jama.2020.17021

Uveges, M. K., Milliken, A., & Alfred, A. (2019). Role of the critical care nurse in disclosing difficult news. *AACN advanced critical care*, *30*(3), 287-293. https://doi.org/10.4037/aacnacc2019436

Villar, J., Ferrando, C., Martínez, D., Ambrós, A., Muñoz, T., Soler, J. A., … Soro, M. (2020). Dexamethasone treatment for the acute respiratory distress syndrome: a multicentre, randomised controlled trial. *The Lancet Respiratory Medicine*, *8*(3), 267–276. https://doi.org/10.1016/S2213-2600(19)30417-5

Walkey, A. J., Summer, R., Ho, V., & Alkana, P. (2012). Acute Respiratory Distress Syndrome: epidemiology and management approaches. *Clin Epidemiol*, *4*, 159–169.