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SYSTEMATIC REVIEW

Impact of New Ventilation and Hemodynamic Support Strategies on the Recovery of Critically Ill Patients with Acute Respiratory Distress Syndrome due to Sepsis: A Systematic Review

Impacto de las nuevas estrategias de ventilación y soporte hemodinámico en la recuperación de pacientes críticos con síndrome de dificultad respiratoria aguda por sepsis: una revisión sistemática

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ABSTRACT

Acute Respiratory Distress Syndrome (ARDS) is a complication caused by sepsis and present burden in critical care with high mortality and limited effective treatments. Advances in ventilation and hemodynamic support offer potential to improve recovery. Our aim is to systematically evaluate impact of new ventilation and hemodynamic strategies on the recovery of critically ill patients with ARDS due to sepsis. The research is conducted on Web of Science, PubMed, Embase, and Cochrane Library from January 2000 to December 2023. We selected randomized controlled trials and observational studies that looked at adult ARDS patients with sepsis as the main cause were the main focus of the inclusion criteria. Advanced fluid management, extracorporeal membrane oxygenation (ECMO) and lung-protective ventilation were among the interventions. Survival rates, length of mechanical breathing oxygenation improvements and complication rates were among the outcomes examined. Low tidal volume ventilation reduced mortality from 31 % to 40 % and ventilator-induced lung injury. Research stated that prone positioning improved oxygenation and reduced mortality in moderate-to-severe ARDS. We documented ECMO offered survival benefits in refractory cases while conservative fluid strategies reduced ventilator days without impacting mortality. Advanced hemodynamic monitoring and titration improved perfusion and recovery. Certain interventions such as high-frequency oscillatory ventilation, showed limited benefit or increased risk. Emerging strategies in ventilation and hemodynamic support enhance outcomes in sepsis-induced ARDS through individualized care. Future research should refine these interventions to optimize recovery while minimizing risks.

Keywords: Acute Respiratory Distress Syndrome; Sepsis; Ventilation Strategies; Hemodynamic Support;

Systematic Review.

RESUMEN

El Síndrome de Dificultad Respiratoria Aguda (SDRA) es una complicación causada por la sepsis y la carga presente en cuidados intensivos con alta mortalidad y tratamientos efectivos limitados. Los avances en ventilación y soporte hemodinámico ofrecen potencial para mejorar la recuperación. Nuestro objetivo es evaluar sistemáticamente el impacto de las nuevas estrategias ventilatorias y hemodinámicas en la recuperación de pacientes críticos con SDRA por sepsis. La investigación se lleva a cabo en Web of Science, PubMed, Embase y Cochrane Library desde enero de 2000 hasta diciembre de 2023. Se seleccionaron ensayos controlados aleatorios y estudios observacionales que analizaron pacientes adultos con SDRA con sepsis como causa principal, fueron el enfoque principal de los criterios de inclusión. El manejo avanzado de líquidos, la oxigenación por membrana extracorpórea (ECMO) y la ventilación pulmonar protectora fueron algunas de las intervenciones. Las tasas de supervivencia, la duración de la respiración mecánica, las mejoras en la oxigenación y las tasas de complicaciones estuvieron entre los resultados examinados. La ventilación de bajo volumen corriente redujo la mortalidad del 31 % al 40 % y la lesión pulmonar inducida por el ventilador. Las investigaciones indicaron que la posición prona mejoró la oxigenación y redujo la mortalidad en el SDRA de moderado a grave. Documentamos que la ECMO ofrecía beneficios de supervivencia en los casos refractarios, mientras que las estrategias conservadoras de líquidos redujeron los días de uso del ventilador sin afectar la mortalidad. La monitorización y titulación hemodinámica avanzada mejoró la perfusión y la recuperación. Ciertas intervenciones, como la ventilación oscilatoria de alta frecuencia, mostraron un beneficio limitado o un aumento del riesgo. Las estrategias emergentes en ventilación y soporte hemodinámico mejoran los resultados en el SDRA inducido por sepsis a través de la atención individualizada. Las investigaciones futuras deben refinar estas intervenciones para optimizar la recuperación y minimizar los riesgos.

Palabras clave: Síndrome de Distrés Respiratorio Agudo; Sepsis; Estrategias de Ventilación; Soporte Hemodinámico; Revisión Sistemática.

INTRODUCTION

Acute Respiratory Distress Syndrome (ARDS) is induced through sepsis and cause rapidly evolving clinical challenges often resulting in severe complications and high mortality rates. Sepsis is defined as dysregulated host response to infection and remains one of the leading causes of death in critically ill patients globally.[(1)] Morbidity associated with sepsis is staggering with approximately 48,9 million cases recorded worldwide. In 2017 alone statistical evaluations revealed it is leading to 11 million deaths accounting for nearly 20 % of global mortality. Institute for Health Metrics and Evaluation (IHME) estimates global incidence of sepsis stands at 437 cases per 100 000 person-years with sepsis accounting for approximately 6 % of hospital admissions in the United States. This much increase of burden is further compounded by its sequelae Sepsis-Induced Acute Lung Injury (S-ALI) which affects up to 68 % of sepsis patients and significantly worsens their prognosis. The pathophysiology of S-ALI is multifactorial involving inflammatory, oxidative stress, coagulation and genetic mechanisms.[(2)] Endothelial and epithelial damage in the lungs leads to increased permeability of the alveolar-capillary barrier which in turn promotes protein-rich pulmonary edema and impaired gas exchange. Multi-organ failure, respiratory distress, and severe hypoxemia are examples of clinical symptoms. The presence of S-ALI is linked to a much greater mortality rate than non-septic ARDS, with mortality rates in sepsis patients with ALI exceeding 40 %.[(3)] Numerous studies have documented this glaring discrepancy for instance 90-day mortality rate for sepsis-related ALI in an ICU patient group was 35,5 % whereas the rate for non-septic cases was 22,6 %. Strategies centered on early management, ventilatory support and anti-inflammatory medications are being used to lessen the burden of S-ALI or S-ARDS. Better therapeutic approaches and thorough understanding of the disease's biology are needed. Significance of ongoing research and clinical attention on sepsis-induced ARDS is highlighted by its high prevalence-related consequences and dearth of viable therapies.[(4)]

AIM: The aim is evaluating how new ventilation and hemodynamic support strategies impact the recovery of ARDS patients with sepsis. We aim to assess the effectiveness of advanced treatments like lung-protective ventilation, ECMO and improved fluid management in improving patient outcomes, survival, and overall recovery.

METHOD

This systematic review of new study designs involved randomized controlled trials, cohort and observational studies of new strategies for mechanical ventilation and HP in critically ill patients with ARDS due to sepsis. Selection criteria used the fact that the target adult patients (mean age, ≥18 years) had ARDS that complied with the Berlin Definition, and sepsis was the primary reason. This work only considered articles published during the period between January 2000 and December 2023 as part of the search strategy. In the database, some of the considered databases are provided by Web of Science, PubMed, Embase and Cochrane Library. These approaches were used with Boolean operators and MSC terms in order to increase chances of obtaining comprehensiveness of sources with needed information.

Table 1. Search keywords

Primary Terms	Secondary Terms
"Acute Respiratory Distress Syndrome"	"Sepsis-Induced Acute Lung Injury"
"Ventilation Strategies"	"Lung-Protective Ventilation"
"Hemodynamic Support"	"Extracorporeal Membrane Oxygenation"
"Sepsis"	"ARDS Management in Sepsis"
Main string	("Acute Respiratory Distress Syndrome" OR "ARDS") AND ("Sepsis" OR "Sepsis-Induced Acute Lung Injury") AND ("Ventilation Strategies" OR "Lung-Protective Ventilation" OR "Low Tidal Volume") AND ("Hemodynamic Support" OR "Extracorporeal Membrane Oxygenation" OR "ECMO" OR "Fluid Management") NOT ("Non-Septic ARDS" OR "Pediatric Patients")

Data Extraction and Quality Assessment

Two of the authors conducted the preliminary selection based on the titles and abstracts of the studies and then based on the inclusion criteria the full text articles were retrieved and examined. Data collection and extraction were guided by specific inclusion and exclusion features such as study type, participant characteristics, exact type and dose of the intervention, and endpoints. Inadequate agreement was addressed by coming to a consensus or by the intervention of a third assessor.

The risk of bias of individual studies was determined where; Cochrane RoB 2 for RCTs and Newcastle Ottawa scale for observational studies. Bias domains assessed included randomization, treatment crossovers or protocol deviations, and outcomes assessment. Only the highest quality of studies was included for the synthesis. Only quantitative tabular data were gathered and meta-analysis was done wherever possible; the effect size is presented as Risk Ratio (RR) or Mean Difference (MD) with 95 % confidence intervals (CIs). Consistency was evaluated by the I^2 statistic in order to measure heterogeneity. In case of analyzing qualitative sense outcomes, narrative synthesis was caring out, the main focus of which is the tendency and clinical suitability.

Table 2. Evaluation of the quality of the consulted articles

Author(s) and Year	D1	D2	D3	D4	D5
Grotberg JC, Reynolds D, Kraft BD (2023)	Low	Medium	Low	Medium	High
Miller AG, Tan HL, Smith BJ, Rotta AT, Lee JH (2022)	N/A	Medium	Low	Low	Medium
Estrella-Alonso A, Silva-Obregón JA, Fernández-Tobar R, Marián-Crespo C, et al. (2024)	Low	Low	Low	Low	Low
Chiumello D, Fioccola A (2024)	Medium	Medium	Low	Medium	Medium
Battaglini D, Fazzini B, Silva PL, Cruz FF, et al. (2023)	Low	Low	Low	Medium	Low
Khokher W, Malhas SE, Beran A, Iftikhar S, et al. (2022)	Low	Medium	Low	Medium	Medium

This review followed the PRISMA guidelines to ensure transparency and replicability. A PRISMA flow diagram was included to detail the screening and selection process.

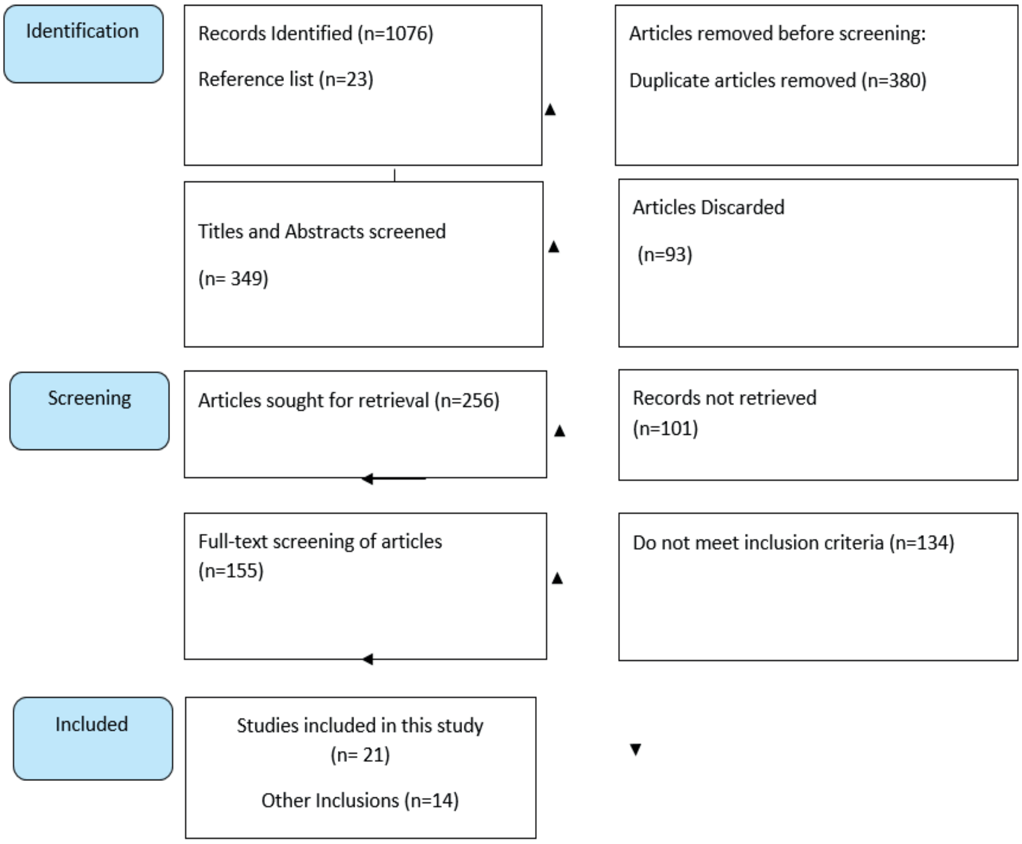

Figure 1. PRISMA Compliance

RESULTS

Table 3. New Ventilation and Hemodynamic Support Strategies in the Recovery of Critically Ill Patients with Acute Respiratory Distress Syndrome (ARDS) due to Sepsis

Strategy	Advancement	How It Works
High-Flow Nasal Cannula (HFNC)	Enhanced oxygen delivery and comfort	Provides heated, humidified oxygen at higher flow rates to improve oxygenation and reduce work of breathing.
Non-invasive Positive Pressure Ventilation (NIPPV)	Improved patient tolerance, decreased intubation rates	Delivers positive pressure during inspiration and expiration, improving gas exchange and reducing ventilator dependency.
Prone Positioning	Increased use in awake patients and less sedation	Shifts the lung perfusion and ventilation balance, improving oxygenation by redistributing lung fluids and expanding ventral lung regions.
Mechanical Ventilation with Adaptive Support	Personalized settings using advanced monitoring	Adjusts ventilator settings based on real-time feedback from respiratory mechanics, optimizing tidal volumes and minimizing barotrauma.
Extracorporeal Membrane Oxygenation (ECMO)	Enhanced use for refractory hypoxemia	Oxygenates blood outside the body, allowing lung rest and healing in severe ARDS patients who do not respond to conventional ventilation.
Inhaled Nitric Oxide (in)	Improved pulmonary vasodilation	Inhaled nitric oxide helps reduce pulmonary vascular resistance and improves oxygenation by targeting pulmonary vasculature.
Vasopressor and Inotropic Therapy	Use of newer agents and combination therapies	Optimizes hemodynamic support to restore and maintain adequate organ perfusion, improving outcomes in septic ARDS.
Pulmonary Rehabilitation Post-Ventilation	Early, targeted rehabilitation programs	Facilitates lung recovery by improving respiratory muscle strength and function, reducing long-term ventilation dependence.
Titrated Sedation Protocols	Sedation minimization, enhanced patient-ventilator synchrony	Aims for lighter sedation levels to improve patient comfort, reduce delirium, and enhance respiratory mechanics.

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Table 4. Results Mechanical Ventilation Strategies in ARDS

Category	Key Findings	References
Low Tidal Volume Ventilation (LTVV) [5,6]	LTVV (6 cc/kg IBW) improves mortality (31 % vs. 40 %) and increases ventilator-free days. LTVV reduces driving pressure and volutrauma but may cause barotrauma in noncompliant lungs. VC mode prioritizes tidal volume; PC mode prioritizes airway pressure.	Culnan., 2018 and Weiss., 2016
Ventilator Asynchrony [7]	Asynchrony index (AI) > 10 % is linked to increased ICU and hospital mortality. Triggering, cycling, and flow asynchronies are common, each with tailored remedies (e.g., sensitivity adjustments, inspiratory time changes).	Francis., 2021
Positive End-Expiratory Pressure (PEEP)[8]	No universal mortality benefit with high PEEP; benefits observed in moderate-to-severe ARDS, especially in PEEP-responsive patients. Advanced titration methods: Stress Index, Electrical Impedance Tomography, and Esophageal Manometry. Individualized PEEP considers oxygenation, compliance, and hemodynamics.	Sahetya., 2017
Recruitment Maneuvers [9]	Improve oxygenation but not mortality; associated with risks like hypotension and cardiac events. ART trial showed increased mortality with aggressive recruitment maneuvers. Recommended only in select patients using stepwise PEEP titration over sustained inflation.	Cui., 2020
Driving Pressure [10]	High driving pressure (>15–17 cm H2O) correlates with increased mortality. Adjusting tidal volume for compliance (rather than IBW) optimizes outcomes. Target driving pressure <15 cm H2O for reduced mortality.	Zaidi., 2024

Table 5. Key Findings

Category	Key Findings	References
Airway Pressure Release Ventilation (APRV) [11]	Improves oxygenation and ICU stay; mixed results on mortality. Lacks high-quality evidence; better outcomes in some ARDS subgroups; TCAV may optimize parameters.	Grothberg., 2023
High-Frequency Oscillatory Ventilation (HFOV) [12]	Mixed results in ARDS; associated with improved mortality in severe ARDS but worsened outcomes in mild-to-moderate ARDS. Societies advise against routine use.	Miller., 2022
Mechanical Power [13]	Higher mechanical power correlates with increased mortality and decreased ventilator-free days; driving pressure and RR are key predictors of ventilator-induced lung injury (VILI).	Paudel., 2021
Proning [14]	Reduces mortality in moderate-to-severe ARDS; PROSEVA trial demonstrated significant survival benefit; duration ≥12 h/session is most effective.	Estrella-Alonso., 2024
Fluid Management[15]	Conservative fluid strategy reduces ventilator and ICU days without affecting mortality; POCUS aids hemodynamic assessment but IVC variation is unreliable in ARDS.	Chuimello., 2024
Glucocorticoids [16]	Dexamethasone improves mortality in COVID-19 ARDS; benefits vary by ARDS phenotype (hyperinflammatory vs. hypoinflammatory). Empiric use remains controversial.	Battaglini., 2023
Neuromuscular Blockade (NMB)[17]	Improves oxygenation but inconsistent mortality benefits; prolonged use increases risks (e.g., weakness, sedation effects). Train-of-four monitoring optimizes dosing.	Davis., 2021
Inhaled Pulmonary Vasodilators [18]	Improve oxygenation and P/F ratio but do not improve mortality; limited to refractory hypoxemia.	Khokher., 2022
Veno-Venous ECMO[19]	Shown to improve outcomes in select patients; CESAR and EOLIA trials indicate survival benefits but with significant variability based on patient selection.	Orthmann., 2023

Mechanical Ventilation Strategies in ARDS

Sepsis induced ARDS has continued to be a major challenge among critically ill patients admitted to Intensive care units. In recent years, the approaches that enhances the ventilation and hemodynamic support have created a breakthrough in management of sepsis induced ARDS. The High-Flow Nasal Cannula (HFNC) and Non-invasive Positive Pressure Ventilation (NIPPV) conserve airway patency without invasively intervening, although their efficacy in significant ARDS is disputed. There is highly significant evidence supporting prone position in increasing lung perfusion and improving oxygenation in otherwise difficult to manage ARDS such as those stemming from sepsis.[6-19]

Mechanical ventilation with adaptive support allows tailored settings based on real-time respiratory feedback reducing ventilator-induced lung injury. When the case is severe, Extracorporeal Membrane Oxygenation (ECMO) is used to provide oxygenation while allowing lung rest though its high risk profile limits its use to refractory cases. Inhaled nitric oxide (iNO) aids oxygenation by reducing pulmonary vascular resistance but it is clinical utility remains debated due to cost and limited evidence on long-term outcomes. Vasopressors and inotropes are critical for stabilizing hemodynamics in septic ARDS while pulmonary rehabilitation improves long-term recovery post-ventilation. Titrated sedation protocols more focus on lighter sedation and help reduce delirium and accelerate recovery, although these strategies show promise but their efficacy depends on individualized patient characteristics which means there is need of ongoing research and clinical refinement. Evolving ventilation strategies such as low tidal volume ventilation (LTVV), have shown clear benefits in reducing mortality and enhancing recovery for instance ARMA trial showed mortality reduction from 40 % to 31 % when employing LTVV (6 cc/kg IBW) compared to traditional tidal volumes (12 cc/kg IBW). Approach mitigates ventilator-induced lung injury (VILI) by reducing volutrauma and barotrauma though issues like ventilator asynchrony and deeper sedation requirements necessitate careful patient monitoring. Ventilator asynchrony when unaddressed if will worsen outcomes and can cause increase of ICU and hospital mortality rate. Asynchrony indices above 10 % indicate the necessity for specialized interventions such as changing inspiratory intervals to prevent cycling asynchrony or adjusting trigger sensitivity to cause asynchrony. Studies shows that synchronization can be greatly enhanced by proactive management of flow asynchrony such as switching to pressure control ventilation.[6-19] Particularly in moderate-to-severe ARDS, positive end-expiratory pressure (PEEP) is crucial for preserving alveolar recruitment and averting collapse. High PEEP helps PEEP-responsive patients however it does not always lower mortality. Electrical impedance tomography and esophageal manometry are two personalized PEEP titration techniques that have the potential to maximize lung compliance and oxygenation. But these strategies haven't always shown advantages for survival. Although the goal of recruitment techniques is to reopen atelectatic lung areas, their use is still debatable. Aggressive recruitment strategies were associated with higher mortality in the ART study mainly because they compromised hemodynamics. Particularly for patients at high risk of hemodynamic instability, safer stepwise PEEP titration techniques are advised over prolonged inflated maneuvers. Without influencing mortality, the conservative fluid management has shown significant advantages in lowering ventilator-free days and intensive care unit stays. Trials like FACTT have a strong emphasis on preventing fluid overload which worsens lung injury and maintaining lower central venous pressures. Limits of conventional metrics, such as inferior vena cava variability, are overcome by contemporary instruments like point-of-care ultrasound (POCUS) which offer dynamic evaluations of fluid responsiveness. Methods for calculating the left ventricular outflow tract velocity-time integral (LVOT VTI) provide more accurate recommendations for fluid treatment optimization. In patients with ARDS, driving pressure a crucial factor in lung strain and is directly correlated with death. Results are poorer when values are higher than 15–17 cm H2O. VILI and mechanical power are decreased by modifying ventilatory settings to reach driving pressures below this cutoff. In order to mitigate lung injury, strategies that prioritize compliance-adjusted tidal volume over IBW-based techniques are essential. Prone positioning and inhaled pulmonary vasodilators are examples of adjunctive therapies that offer extra resources for treating severe acute respiratory distress syndrome. When sustained for at least 12 hours per session, proneness lowers mortality in moderate-to-severe instances, as confirmed by the PROSEVA experiment. Nitric oxide and other inhaled vasodilators increase oxygenation, but there is little proof that they improve survival, therefore their use is limited to refractory hypoxemia.[6-19] Neuromuscular blockade (NMB) improves oxygenation but its inconsistent impact on mortality and associated risks like it may lead to critical illness myopathy and require judicious application. Monitoring tools like train-of-four assist in optimizing dosing and minimizing complications. Veno-venous extracorporeal membrane oxygenation (V-V ECMO) is one of the well-recognized rescue strategies for patients with refractory hypoxemia. The CESAR and EOLIA trials demonstrate survival benefits in carefully selected populations although its high resource demands and potential complications signify importance of stringent patient selection. Survivors of ARDS often face prolonged physical and neurocognitive impairments.[20,21] Research shows chronic impairments in exercise capacity, lung function and health-related quality of life that last for years. Within the first year after discharge, more than half of survivor's experience cognitive impairment and psychiatric morbidities such as sadness and PTSD. Early mobilization and rehabilitation interventions could lessen these long-term effects. Incidence of 25–38 % in severe ARDS, acute cor pulmonale (ACP) has a substantial effect on results and early detection of right ventricular (RV) dysfunction is made possible by echocardiographic monitoring which directs treatments such as pulmonary vasodilators and customized PEEP techniques. Efficient regulation of fluid balance, inotropic support and RV afterload is crucial for reducing the negative consequences of high pulmonary vascular resistance.[22,23] There has been a dramatic improvement in the management of critically ill patients suffering from acute respiratory distress syndrome ARDS of septic etiology due to recent developments in ventilation and hemodynamic support strategies. High-Flow Nasal Cannula, HFNC, and Non-invasive Positive Pressure Ventilation, NIPPV, are non-invasive forms of oxygenation that lessen the need for intubation, although their application in severe ARDS is controversial. Prone positioning has proven effective in the redistribution of lung perfusion, thereby enhancing oxygenation in refractory forms of ARDS such as that caused by sepsis.[24] Adaptive support Mechanical ventilation is more effective, as ventilator settings are adjusted according to the patient's current respiratory feedback, thereby minimizing ventilator-associated lung injury. In the worst of cases, ECMO, or Extracorporeal Membrane Oxygenation can be deployed to oxygenate the body while permitting lung rest, however due to the risk profile of this technique, it can only be used in refractory cases. NO inhalation reduces pulmonary vascular resistance and, therefore, helps with oxygenation. However, the anti-inflammatory effects are not enough to justify the expense and availability of conclusive proof describing long term use of the technique.

Vasopressor and inotropic agents are fundamental for achieving hemodynamic stability in septic ARDS patients, and pulmonary rehabilitation enhances post-ventilation long term recovery. Titration of sedatives to daze the patient less, and focus more on light levels of sedation, allows for a decrease in delirium and thus enable faster recovery. While these measures appear to work, such effectiveness is dependent on factors concerning the individual mechanics of the patient. Thus, further studies are required, as well as clinical tuning and adjustments.[25] The research says that genetic polymorphisms in the Xanthine oxidoreductase gene (XOR) are associated with sepsis and ARDS risk with higher serum XOR activity serving as a potential biomarker for prognosis in diverse populations.[26] Knockdown of ASLNC12002 reduced epithelial-mesenchymal transition (EMT) in sepsis-induced ARDS indicating its potential as a therapeutic target for preventing pulmonary fibrosis.[27] CircN4bp1 is another key biomarker which was found to promote M1 macrophage polarization and contributing to inflammation in sepsis-induced ARDS. Silencing circN4bp1 alleviated lung injury and inflammation while suggesting its potential as a therapeutic strategy. In addition, a study identified that MX1+ natural killer cells exacerbated the progression of sepsis-induced ARDS by promoting an inflammatory response providing a new target for therapeutic intervention.[28] A retrospective study on septic shock and respiratory distress found no impact of intubation on hospital mortality but highlighted higher ICU and hospital mortality along with more hospital-free days for intubated patients. A randomized clinical trial comparing ventilation strategies (pressure control vs. volume assist-control) in ARDS showed no significant differences in hospital mortality or ventilator-free days but the pressure-controlled group required fewer adjunctive therapies. Another study on personalized PEEP levels in ARDS found no correlation between two methods of determining optimal PEEP, with distinct results in pulmonary vs. extra pulmonary ARDS.[29,30] As the LUNG SAFE study looking at CO2 management strategies in ARDS patients points out, there was no definitive correlation between CO2 levels and mortality rates. However, patients from middle-income countries experienced sustained hypocapnia more frequently.[31,32,33] Another study concerning ECMO in ARDS suggested that both older age and higher ventilatory pressures were associated with higher mortality. The PHARLAP trial, directed at finding effective recruitment techniques, found no difference between the two groups with regard to ventilator-free days or mortality but there was a decrease in adjuvants therapy in the intervention group. Similarly, the trial on neuromuscular blockade in ARDS showed no efficacy in mortality improvement, but a study on ARDS-attributable mortality had shown an increase in sepsis-associated ARDS patients. This evidence suggests that genetic polymorphisms, circN4bp1 and MX1+ natural killer cells might function as innovative mechanisms applicable to therapeutic strategies for sepsis-induced ARDS. Several studies also suggest that PEEP methods, PEEP ventilation strategies, and sivelestat have plausible benefits in ARDS management but mortality benefit was not found.[34,35]

CONCLUSION

Currently, with the improvement brought about in the understanding of ventilation strategies and hemodynamic support strategies, the management of acute respiratory distress syndrome (ARDS) due to sepsis has improved considerably. High-Flow Nasal Cannula (HFNC) and Non-invasive Positive Pressure Ventilation (NIPPV) are forms of non-invasive oxygen support that do not eliminate the need for intubation, although their role in severe ARDS management is still contested. Prone positioning has been demonstrated to be effective in ameliorating the fused lung perfusion and facilitates oxygenation in oxygenation in skilled refractory in situ ARDS including the post septic state. Adaptive Support Ventilation prevents the micromechanical injuries which are caused by providing rigid and set mechanical parameters for the mechanical ventilators. ECMO is commonly used in extreme cases as a means of providing oxygenation whilst resting the lungs however due to its high-risk profile it does have its reservations. Inhaled nitric oxide (iNO) authorizes oxygenation when pulmonary vascular resistance is undertaken. Its utility however in clinical settings at present is still contested owing to high cost involved coupled with lack of evidence explaining long term outcomes. Vasopressors and inotropic agents are important in the management of septic ARDS in terms of controlling hemodynamics and bilateral pars-alternation ventilator doses effect pulmonary rehabilitation in the long term. Controlled sedation, particularly light sedation enables the hemostasis.

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