

Open Access

Article Information

Received: August 5, 2023

Accepted: August 23, 2024

Published: August 31, 2024

Keywords

Pneumonia,
Ventilation,
Mechanical ventilation,
Lungs,
Sacs.

Authors' Contribution

AJA conceived and designed the study; AJA and MAA wrote the first draft of the manuscript; DMA, AMA and AMA revised the manuscript, and AJA approved the final manuscript.

How to cite

Alkhatib, A.J., Al-Shehabat, M.A., Al-Shehabat, D.M., Al-Shehabat, A.M., Al-Shehabat, A.M., 2024. Exploring the Impact of Pneumonia on Mechanical Ventilation. *Int. J. Mol. Microbiol.*, 7(2): 83-100.

***Correspondence**

Ahed J Alkhatib
Email: ajalkhatib@just.edu.jo

Possible submissions



[Submit your article](#)

Exploring the Impact of Pneumonia on Mechanical Ventilation

Ahed J Alkhatib^{*1,2,3}, Mustafa Ahmad Al-Shehabat⁴, Dania Mustafa Al-Shehabat⁵, Aya Mustafa Al-Shehabat⁶, Adam Mustafa Al-Shehabat⁶

¹Department of Legal Medicine, Toxicology and Forensic Medicine, Jordan University of Science & Technology, Jordan.

²International Mariinskaya Academy, department of medicine and critical care, department of philosophy, Academician secretary of department of Sociology.

³Cypress International Institute University, Texas, USA.

⁴Department of Physiology and Biochemistry, Faculty of Medicine, Jordan University of Science and Technology, Jordan.

⁵King Abdulla University Hospital, Jordan.

⁶Faculty of Medicine, Jordan University of Science & Technology, Jordan.

Abstract:

Pneumonia, an infection leading to inflammation of air sacs present in one or both lungs, commonly causes symptoms such as cough, chest pain, fever, and breathing difficulty. The main objective of the present study was to review the updates of cited literature regarding the impact of pneumonia on mechanical ventilation. To achieve this objective, the researcher referred to the most popular search engines, such as PubMed, Google Scholar, Science Direct, and others. This review indicated that pneumonia and mechanical ventilation are important topics in medicine, particularly emergency medicine.



Scan QR code to visit
this journal.

©2024 PSM Journals. This work at International Journal of Molecular Microbiology; ISSN (Online): 2617-7633, is an open-access article distributed under the terms and conditions of the Creative Commons Attribution-Non-commercial 4.0 International (CC BY-NC 4.0) licence. To view a copy of this licence, visit <https://creativecommons.org/licenses/by-nc/4.0/>.

INTRODUCTION

Pneumonia, an infection leading to inflammation of air sacs present in one or both lungs, commonly causes symptoms such as cough, chest pain, fever, and breathing difficulty (Janssens *et al.*, 2021). In some cases, especially in severe pneumonia, the patient may require respiratory support in the form of mechanical ventilation for the maintenance of adequate oxygenation and ventilation (Huang *et al.*, 2022). Pneumonia requiring ventilatory support may encompass a diverse nature of microbial hosts, strengths, types of lung infiltration like bronchopneumonia, lobar pneumonia, complicated and non-complicated pneumonia, and last but not least, the host's state of immunity. Each of these variants opens a new level of complexity and creates a unique set of challenges not just for the physician, but also for the nursing professionals attending to such patients (Rackley, 2020). This point of view draws attention to the following points: reasons, why some obstruct the ventilation of one or both lungs, and influence other body parts, thereby causing systemic problems, for example, affecting heart function, leading to other body parts not getting a sufficient supply of oxygen to perform their normal function, the contrasting beliefs of patients and physicians, and a brief overview of ventilator-associated pneumonia (Broadhurst *et al.*, 2022; Gosangi *et al.*, 2022; Karunarathna *et al.*, 2024b; Karunarathna *et al.*, 2024d).

Mechanical ventilation is done when enough oxygen is not delivered to the body owing to very slow or no breathing or to reduce work imposed on overstressed muscles in patients with infectious illnesses or patients who cannot move (Nascimento-Carvalho, 2020). Most patients with community-acquired pneumonia can be managed on an outpatient basis, while others who have severe pneumonia, pneumonic consolidation on chest X-ray, known or chronic heart/lung disease, or compromised immunity benefit from either invasive mechanical ventilation, noninvasive positive pressure ventilation, or high-flow oxygen therapy (Andersen and Pant, 2022). Healthcare

professionals managing patients with pneumonia who require ventilatory assistance face a peculiar set of challenges, the most important of which is to balance between ventilation and ventilator injury, including ventilator-associated pneumonia (Jones *et al.*, 2020). More often than not, the patients are already very sick, wherein the antibacterial used is based on personal and institutional beliefs without considering the local immune status of the pneumonia-promoting microbial entity likely to be causing pneumonia in particular; their beliefs about the probable cause of pneumonia are mostly in contrast to each other (Rejas *et al.*, 2022). A vigorous set of pathophysiological and traditional microbiological studies has come out with certain labeled findings such that the reason pneumonia patients tend to have a higher heart rate is due to reduced carbon dioxide elimination in severe, life-threatening respiratory failure states. Pneumonia due to bacteria has different clinical severity related to host resistance for the same species. In some cases, consolidation or incursion in lung percussion changes on chest examination may be completely different (Tillotson *et al.*, 2020).

Pathophysiology of Pneumonia

Pneumonia is a bacterial infection that incites significant inflammation and damage to the lungs (Long *et al.*, 2022). Although viral infections also lead to damage of a similar extent, much of the damage from acute respiratory viral pandemics is indirect and brought on by the immune system (Kumar, 2020). The underlying symptoms of pneumonia, including productive cough, fever, and malaise, relate to the body's immune response to the organisms, as much as they do to the organisms themselves (Stotts *et al.*, 2023). Macrophages and neutrophils begin to attack the pathogens in acute pneumonia. The injured cells of the alveoli are incapable of protecting the tissue further. They further release proteases and inflammatory substances that damage the tissue (Land, 2021). This inflammation can reduce lung volume, and lung compliance, and cause life-threatening respiratory failure. Lung injury then leads to a number of significant

pathophysiological changes. Defense against bacteria during acute pneumonia results in inflammatory septal damage (Badraoui *et al.*, 2021). This inflammation and the increased pressure in the alveoli allow fluid to move into the tissue from the blood and alveoli (Lara *et al.*, 2020). The body's ability to maintain the pressure and provide oxygen to the blood through the tissue is reduced (Land, 2021). Damage to the alveolar-capillary membrane ensues with eventual disruption of the cytoskeleton and cell death (Badraoui *et al.*, 2021). Pulmonary shunts may develop at this stage. Factors that affect the competition of pro-inflammatory substances or the inhibition of their release determine the amount of lung injury in various types of pneumonia (Al-Saghir *et al.*, 2015). Pulmonary shunting relates to the release of cytokines and other pro-inflammatory substances, making the hypoxia in ARDS refractory to increases in airway pressure. The development of hypoxemia in pneumonia underscores the degree to which this process has occurred (Mondeshki *et al.*, 2022).

Inflammatory Response

Pneumonia is a severe infection of the lung that poses an important burden for healthcare systems across the globe (Long *et al.*, 2022). The lung and its defense mechanisms are frequently affected by bacterial pneumonia. The immune system initially recognizes when its barriers to infection are breached by newly arrived pathogens (Huang *et al.*, 2022). Following the invasion of the alveolar space by commensal or nosocomial pathogens, a variety of sentinel immune cells become involved, including alveolar macrophages, type 2 alveolar cells, and dendritic cells (Waterer, 2021). These cells, through a panoply of pattern recognition receptors, start to release inflammatory mediators, including chemokines, cytokines, lipid metabolites, and interferons (Mah *et al.*, 2022). Such signaling cascades recruit and manipulate other leukocytes to a point where they can impede the aggressor's replication or engulf and destroy it (Longhitano *et al.*, 2021). Signaling can either be via immune cells directly confronting pathogens in the alveoli of

pneumonia patients or indirectly ensheathing them within a biofilm until the effective release of mucus and clearance occurs (Fonseca *et al.*, 2021). Despite these myriad cascades of events, pneumonia is still possible (Izumi and Akifusa, 2021). That is to say, the collateral damage caused to lung structure and function by aggressive leukocyte effectors and the quantities of mucus summoned for pathogen blockade and removal can compromise lung function to the point of breathing difficulties and excessive gas accumulation (Aithal *et al.*, 2023; Núñez-Fernández *et al.*, 2021).

Inflammation is another impact of the irritants that cause pneumonia, and your mind perceives this as a malfunction (Iqbal, 2021; Stotts *et al.*, 2023). More specifically, it is hyperirritant, causing supersession of the expected response (Kumar, 2020). It is defined physiologically as the center that is inhibited by large doses of drugs dissimilar to those that excite or, in other words, a deceptively simple concept (Waterer, 2021). The current clinical model to diagnose pneumonia utilizes simple clinical and paraclinical information like cough, fever, fast breathing, and diarrhea, whilst emphasizing that it cannot differentiate whether pneumonia is present due to viral or bacterial etiological causes (Sriram *et al.*, 2021). Nevertheless, a proportion of pneumonia-associated alveolar damage is caused when inflammation gets out of control and causes damage to normally resistant alveolar walls (Anderson and Feldman, 2023). This will result in increased work of breathing and the need for mechanical ventilation (Takahashi *et al.*, 2022). One technique to widen the airway and perhaps lessen or even completely eradicate these symptoms is mucolytic medication treatment (Ali *et al.*, 2019).

Alveolar Damage

Pathogens involved in pneumonia affect lung parts already affected by injury, regardless of whether the original cause of injury was viral, physical, or idiopathic (Clementi *et al.*, 2021). Acutely injured alveoli suffer from the overflow of pathogens and their products to the point that

capillaries become engorged (Luyt *et al.*, 2020). The capillary blockade prevents red blood cells carrying oxygen from entering, limiting, and eventually shutting down the gaseous exchange—a pathological mechanism called shunt (Kosutova and Mikolka, 2021). Engorged alveolar capillaries force red blood cells against the capillary wall, where they release their hemoglobin content, including iron, transforming bacteria into active metabolizers with an increased growth rate (Georgakopoulou *et al.*, 2023; Hou *et al.*, 2022; Thibeault *et al.*, 2021). In addition, the accumulation of iron-damaged red blood cells leads to the progressive clearance of heme and iron from the alveoli (Bonaventura *et al.*, 2021).

As the latter are released during the uptake of red blood cells, iron rapidly increases in the alveolar fluid that bathes the lung and elicits potent inflammatory processes (Qureshi and Mustafa, 2018). In addition to the cessation of gas exchange, the result is the destruction of the alveolar walls. Such destruction has profound consequences (Manickavel, 2021). Alveolar walls, directly exposed to the inhaled air, provide the largest possible area for gaseous exchanges to occur, only fractionally thicker than a sheet of paper; their destruction reduces the total area over which exchanges can occur (Mason, 2020). The extent of destruction likely carries important clinical information, providing valuable cues to suggest the ventilatory strategy that should be adopted to treat a correctable problem (Battaglini *et al.*, 2023a; Ramirez-Estrada *et al.*, 2023). Instead of focusing on functional impairment as in pathophysiology, the remaining two paths will dwell on direct mechanisms of tissue injury (Kim *et al.*, 2024). Therefore, attention will be diverted from inflammation to mechanisms (Dimbath *et al.*, 2021; Zeng *et al.*, 2022). Data and far-reaching considerations will alternate with basic research regarding the role of these effectors in injury (Toth *et al.*, 2022).

Mechanical Ventilation in Pneumonia Patients

Mechanical ventilation is an important strategy in the management of patients with pneumonia.

Indications include acute hypoxemic respiratory failure and/or severe sepsis and septic shock with refractory hypotension (Kózka *et al.*, 2020). The clinical importance of these recommendations is that, as hypotension is a common expression of sepsis-induced cardiovascular failure, there is a very limited amount of time available for the reversal of hypoperfusion, the restoration of cardiovascular function, and the treatment of occult hypoxemia (Alkhatib, 2021). Ventilatory settings may be very important for pneumonia (Liaqat *et al.*, 2022). Tidal volume can distribute the alveolar ventilation, oxygen concentration can increase the alveolar oxygen pressure, the ratio of the inspired oxygen concentration, and the average alveolar pressure, and the positive end-expiratory pressure to keep the alveoli open at the end of inhalation, which can influence the alveolar mechanics and the local immunity (Dupuis *et al.*, 2021; Johnstone *et al.*, 2021; Peng *et al.*, 2020; Sánchez-Guijo *et al.*, 2020). The choice of these settings may be influenced by the severity of pneumonia (Meawed *et al.*, 2021).

Correct ventilator strategies for patients with pneumonia are still topics of debate. International recommendations for mechanical ventilation are few (Alkhatib, 2021). The concept of protective mechanical ventilation ensured through dimensioning tidal volume, limiting airway pressure, and ensuring sufficient PEEP seems to be used in clinical practice at any stage of the disease (Papazian *et al.*, 2020). However, when this strategy is applied is deeply subjective and unstandardized (Howroyd *et al.*, 2024). Although a guideline might be considered feasible, it would only state clinical evidence in an average of intermediating physicians, who make many critical decisions, particularly in severe cases (Fally *et al.*, 2024). Typically, a standard evidence-based therapeutic goal is issued, and the degree of severity that describes the population does not apply to individual patients (Fernando *et al.*, 2020). Large-scale clinical studies were performed to observe disease outcomes and mortality in the overall population, including many cases of conservative treatment that had few reasons for

mechanical ventilation (Goligher *et al.*, 2020). Political decisional guidelines propagate the concept that evidence from practice can help correct results, according to timely interventions, hence reducing the impact of chronic disease and the inadequacy of treatment and dose (Windisch *et al.*, 2020). General guidelines have failed to alleviate the ambiguity concerning conservative treatment (Pickens *et al.*, 2021).

Indications for Mechanical Ventilation

Pneumonia is one of the medical conditions that require mechanical ventilation (Kózka *et al.*, 2020). This suggests that it is a requirement for patients with pneumonia who may need ventilator support (Gragueb-Chatti *et al.*, 2021). Indications for mechanical ventilation have to do with an immediate and urgent clinical disentanglement of the patient who needs ventilatory and respiratory assistance (Ebrahimian *et al.*, 2021). The basis for the beginning of the mechanical ventilation of a patient with pneumonia is the clinical condition of acute respiratory failure, in which the immediate initiation of mechanical ventilatory support decreases morbidity, and fiscal costs of the illness, and saves lives most of the time (Marietta *et al.*, 2020). The conditions for the critical patient who may need mechanical ventilation are based on clinical judgment that requires the use of anamnesis, computed tomography, images, and laboratory results indicating the severity of the patient with pneumonia (Umemura *et al.*, 2021). Etiology is another factor in the decision-making for critical patients with pneumonia according to the extended spectrum of the pathogen (Assimakopoulos *et al.*, 2021). Arterial blood gas analysis is the ultimate marker for clinical decision-making in critically ill patients (Lima *et al.*, 2020).

In a patient with community-acquired pneumonia, mechanical ventilation should be initiated very soon in the absence or presence of clinical signs (Nair and Niederman, 2021). The absence of clinical signs includes moderate to severe hypoxemia at room air causing severe hypoxemia with clinical symptoms, the existence

of hypercapnia, and type II respiratory failure confirmed by the PaCO₂ value and the pH value with a severe ratio with HCO₃ (Martin-Loeches *et al.*, 2023b). Clinical signs are represented by the need for airway protection and ventilatory assistance, impending death, clinical symptoms compared with a better-computed tomography image showing a more extensive infiltrate, and other related clinical aspects (Ferrer *et al.*, 2024; Yang and Shu, 2024). It is most important for the discussants and teachers of pulmonology to know the criteria for initiating mechanical ventilation in a patient with pneumonia (Deshpande *et al.*, 2022).

Ventilator Settings

One of the key factors affecting outcomes in mechanically ventilated patients with pneumonia in terms of lung-protective ventilation, which has a positive impact on patients, is the setting and adjustment of the ventilator according to the patient's response (Diehl *et al.*, 2020; Hassan *et al.*, 2021; Liu and Wang, 2022). The aim of mechanical ventilation, especially in patients with pneumonia, is to maintain appropriate gas exchange in the blood, re-expand collapsed lungs, and unload the respiratory muscles until the underlying pathology leading to the need for mechanical ventilation is resolved (Astasio-Picado *et al.*, 2022; Gupta *et al.*, 2021; Hurry, 2024; Lehingue *et al.*, 2022; Pelosi *et al.*, 2022; Wong *et al.*, 2022).

Adjusting ventilator parameters such as tidal volume, respiratory rate, and fraction of inspired oxygen has long been seen as the standard of care in most intubated patients with pneumonia (Grasselli *et al.*, 2021). Starting in 1996, a system began designing static parameters of ventilation that would be lung-protective when applied across groups of patients who had been classified as having ARDS (Rackley, 2020). Moving forward, however, research has shown the need for individual patient care and adjustment of mechanical ventilatory parameters following patient response (Nolley *et al.*, 2023). Although an open lung strategy begins with a minimum value for PEEP, a minimum FiO₂, and setting the tidal volume and respiratory rate to

achieve adequate minute ventilation, actual ventilatory settings and parameters may be repeatedly titrated (Battaglini *et al.*, 2021). Initial ventilator settings in intubated patients appear in a referenced table. Since optimal ventilator settings often lean heavily on the patient's underlying pathophysiology of lung failure, they may be adjusted according to the patient's or the disease process's performance and response to the chosen ventilator parameters (Calligaro *et al.*, 2020; Peña-López *et al.*, 2024).

Overall, restricted tidal volume and plateau pressure are important for ensuring lung protection, but adequate oxygenation and ventilation can only be established if all three parameters are combined, adjusted based on response and outcome, and regularly checked and rechecked throughout the patient's clinical course (Guidet *et al.*, 2024). Baseline ventilator support settings in non-intubated and intubated patients are provided for informational purposes in a referenced table (Duggal *et al.*, 2024; Reynolds *et al.*, 2021). Titration and management of the settings described in the referenced table belong to those professionals experienced in critical care and advanced airway management (Chen *et al.*, 2022; D'Cruz *et al.*, 2023; Motes *et al.*, 2023). Clearly, adjustment of these strategies will rely heavily on factors such as patient response and trajectory of illness, and it is beyond the scope of this document to advise on specific parameters of such strategies, especially with debate about appropriate oxygen targets in the literature (Ewers and Lehmann, 2022; Hess *et al.*, 2020; Hughes *et al.*, 2024).

Complications of Mechanical Ventilation in Pneumonia Patients

Mechanical ventilation may be required in patients with pneumonia due to the worsening of respiratory conditions and in case of failure of noninvasive ventilation support, high-flow oxygen from a nasal cannula, and standard oxygen therapy (Karunaratna *et al.*, 2024a; Pagliano *et al.*, 2021). Mechanical ventilation can be a lifesaving intervention, increasing the possibility of survival in patients with hypoxemic respiratory failure and even in more stable

patients with pneumonia. However, the application of mechanical ventilation can be associated with several complications (MacLeod *et al.*, 2021).

Indeed, it is essential to appreciate that the use of mechanical ventilation involves a potential "so-called vicious circle" where the benefits of mechanical life support are balanced against the iatrogenic complications of intrusive mechanical life support (Patil *et al.*, 2022). In this regard, mechanical ventilation can exacerbate pulmonary inflammation in patients with pneumonia, leading to ventilator-associated pneumonia and the occurrence of barotrauma, air leaks, nosocomial pneumonia, and impaired oxygenation (Bordon *et al.*, 2021). The development of barotrauma and altered lung compliance also increases the risk for supportive care strategies such as prone positioning and increased positive end-expiratory pressure required in some patients (Bai *et al.*, 2022; Ziaka and Exadaktylos, 2021).

Several complications can occur during mechanical ventilation, which may affect outcomes during severe pneumonia (Papazian *et al.*, 2020). Ventilator-associated pneumonia is probably the best studied, and many comprehensive and current guidelines are available for clinicians to aid in the prevention, diagnosis, and management of ventilator-associated pneumonia (Shah *et al.*, 2022). Ventilator-associated pneumonia can lead to an increased intensive care unit length of stay, an increased need for sedation and paralytics, and an increased need for mechanical ventilation in addition to increased morbidity and mortality (Coelho *et al.*, 2023). Peri-intubation-related hypoxemia can occur as a result of aspiration of gastric contents, post-intubation atelectasis, or aspiration of infective respiratory secretions from the upper airway, and increases in driving pressure can lead to an increased risk of pulmonary barotrauma (Luo *et al.*, 2021). Gastric insufflation is the most important risk factor for refractory hypoxemia in a profoundly hypoxemic pneumonia patient (Savary *et al.*, 2020). Other complications of mechanical ventilation include the development of extra-pulmonary organ

dysfunction (Luque-Paz *et al.*, 2021). With improvements in mechanical ventilator technology, the incidence of barotrauma continues to decrease, particularly in COVID-19, whereas that of volutrauma or atelectrauma might be higher in late-presenting COVID-associated pneumonia patients, although whether this is the case will require data from controlled studies (Szarpak *et al.*, 2021).

Ventilator-Associated Pneumonia

Over the past several decades, there has been a significant increase in the number of available data and the range of research surrounding Ventilator-Associated Pneumonia (VAP) (Omwenga, 2020). As such, the understanding of this condition has been greatly enhanced (Llitjos *et al.*, 2021). Herein, VAP is addressed as an isolated entity, despite its broad scope (Cui *et al.*, 2023). VAP denotes the infection of lung parenchyma distal to the trachea and the mainstem bronchus that develops forty-eight hours after the initiation of mechanical ventilation (Peña-López *et al.*, 2022). VAP occurs in fourteen to seventy-six percent of patients subjected to mechanical ventilation, depending on the presence of pneumonia (Tuyambaze and Hakizimana, 2023). Moreover, up to fifty percent of pneumonia cases are receiving mechanical ventilation (Thomas *et al.*, 2021). VAP is unlikely to develop in the absence of pneumonia (Megahed *et al.*, 2021). At the same time, it is the leading infectious complication of patients subjected to mechanical ventilation (Taha *et al.*, 2022). Mechanical ventilation may increase the risk of pneumonia development due to aspiration and interfere with the drainage of oropharyngeal secretions (Tang *et al.*, 2023). Moreover, the endotracheal tube impairs the cough reflex and mucus clearance (Alkhatib and Ababneh, 2021).

The greatest risk factor for developing VAP is the length of time during which the patient remains on mechanical ventilation (Kózka *et al.*, 2020). In addition, all other risk factors contribute to the increase in the time of mechanical ventilation (Núñez *et al.*, 2021). In the presence of pneumonia and undergoing mechanical ventilation, these risk factors could be

subdivided into host-dependent (old age, very young age, immunosuppression, comorbidities, and sepsis) and those induced by the patient reception (antibiotics, sedation, vasopressors), mechanical ventilation (trauma, aspiration), and uncontrolled sources of infection in nine identifiable microbial foci (unsterilized devices and equipment) (Liu *et al.*, 2022). To prevent VAP, potential infectious sources should be addressed (Pawlik *et al.*, 2022). Moreover, the benefits of the microbiological assessment of specimens obtained using non-invasive methods when selecting an appropriate antimicrobial have not been clearly demonstrated (Garnier *et al.*, 2023). A tracheal aspirate should be requested in patients with suspected or proven VAP who are not taking empirical antibiotics (Kepekci, 2020). The rate of VAP in mechanical ventilation patients was relatively high (Li *et al.*, 2020). These cases can result in prolonged hospitalization, increased costs, and declining moral and legal criticisms (Battaglini *et al.*, 2023b). Inappropriate management, frequent diagnostic errors, overuse of antibiotics, and lack of preventive strategies expose more patients to iatrogenic complications (Rosenthal *et al.*, 2023).

Barotrauma

Barotrauma has been described for many years and is based on the injury that any excessive airway pressure during mechanical ventilation can cause in the lung (McGuinness *et al.*, 2020). The high energy delivered as a transmural pressure gradient can force the liquid from the lumen of the alveoli to the interstitial tissue and eventually to the pleural space (Rajdev *et al.*, 2021). A secondary mechanism for barotrauma is the increase in transpulmonary pressure that can directly overcome the yield of the fibroblastic structure of the lung and result in the rupture of the lung (Alkhatib, 2024). Poorly distensible areas do not rupture under increased localized pressure because the ability of the lung to distribute stress protects the alveoli, but under very high pressure they eventually burst as the pressure in the alveoli is greater than their resistance and the average pressure decreases as the neighboring units fall in collapse (Güven *et al.*, 2021). The clinical manifestations of

barotrauma might follow the same clinical presentation of ventilator-associated pneumonia except for hemodynamic instability and frequent cardiovascular collapse (Lodhia *et al.*, 2023). During controlled mechanical ventilation, total barotrauma can result in either pneumothorax or bronchial disruption, while localized barotrauma induced in certain alveoli can result in pneumomediastinum (Mudhar *et al.*, 2022). Emphysematous patients with limited lung-to-pleural adhesion can develop subcutaneous emphysema. Long-term complications including interstitial emphysema, bronchopleural fistula, bronchiectasis, and chronic empyema may occur (Teo *et al.*, 2023). Shallow alveolar recruitment with low VILI ratios may also act as a thrombogenic factor. The above might indicate that pneumonia can be associated with VAP and barotrauma at the same time (Dogrul *et al.*, 2020).

Current Research and Future Directions

The overall interest in research and future directions in the clinical management of pneumonia related to mechanical ventilation is gradually increasing (Sharma *et al.*, 2021). Furthermore, recent studies in this area have highlighted some important findings regarding pneumonia pathophysiology and treatment, including the effect of the proliferative phase of pneumonia on the mechanics and physiology of the respiratory system. In addition, the treatment of pneumonia has been addressed in several high-quality surveys (Karunaratna *et al.*, 2024c). Although continuous progress in ventilatory strategies has been achieved, much remains to be done to improve this often forgotten category of ICU patients; if adequate interest is not paid, their prognosis is often disappointing (Stainer *et al.*, 2021). Different technological innovations in the last year could be an important help towards a new approach to ventilation strategy for this category of patients (Alafif *et al.*, 2021; Strathdee *et al.*, 2023).

Similarly, several clinical trials are ongoing, and if they are successful, they could revolutionize the field of pneumonia-related mechanical

ventilation (Yang and Shu, 2024). As noted in all statements, the perspective set is the point of view of experts in the field, who are usually members of relevant assemblies (Sánchez-Guijo *et al.*, 2020). As indicated, physicians cannot be expected to be experts in all aspects of medicine or implicitly responsible for the care of diseases. In this spirit, perspectives should be written not only by respiratory experts but also by several professionals who are experts in different categories (Liu *et al.*, 2023). In the ICU, several complications are related to the devices and the presence of the endotracheal tube (Martin-Loeches *et al.*, 2023a). The correct management of the airways, which had to be unofficially ensured for a long time during the pandemic, is again one of the main unresolved issues in our discipline (Cilloniz *et al.*, 2023). From this point of view, future perspectives for research should be directed to this aspect as well (Navarra *et al.*, 2020). If we do not start a multidisciplinary approach to the history of the pneumonia process, we could not allow these patients to reach a functional recuperation adequate to guarantee the same cognitive or work performance that they had prior to infection, even after the acute phase (Investigators *et al.*, 2024). The global interest in pneumonia is also part of the panorama of this history (See *et al.*, 2024).

CONFLICT OF INTEREST

Authors hereby declare that they have no conflict of interest.

REFERENCES

- Aithal, S.S., Sachdeva, I., Kurmi, O.P., 2023. Air quality and respiratory health in children. *Breathe.*, 19(2).
- Al-Saghir, M.G., Alkhatatbeh, M.A., Alkhatib, A.J., 2015. Immunohistochemical Localization of *Aspergillus* and p53 in Human Lung Tissues. *Am. J. Mol. Biol.*, 5(4): 117-123.

- Alaif, T., Tehame, A.M., Bajaba, S., Barnawi, A., Zia, S., 2021. Machine and deep learning towards COVID-19 diagnosis and treatment: survey, challenges, and future directions. *Int. J. Environ. Res. Public Health*, 18(3): 1117.
- Ali, Q., Mafeng, L., Anchun, C., 2019. Use of Bromhexine in the Management of Respiratory Diseases in Chickens. *PSM Microbiol.*, 4(4): 83-87.
- Alkhatib, A.J., 2021. The role of the emergency department in the early management of sepsis. *J. Int. Med. Res. Health Sci.*, 1: 19-23.
- Alkhatib, A.J., 2024. Therapeutic Potential of Fresh Pomegranate in the Management of Pulmonary Fibrosis. *PSM Microbiol.*, 9(1): 1-6.
- Alkhatib, A.J., Ababneh, S.K., 2021. The Impacts of Cigarette Smoking on Rats Trachea-A Histologic Study. *Biomed. J. Sci. Tech. Res.*, 38(1): 30006-30010.
- Andersen, M., Pant, A., 2022. Effects of utilization management on health outcomes: evidence from urinary tract infections and community-acquired pneumonia. *Expert. Rev. Pharmacoecon. Outcomes Res.*, 22(6): 981-992.
- Anderson, R., Feldman, C., 2023. The global burden of community-acquired pneumonia in adults, encompassing invasive pneumococcal disease and the prevalence of its associated cardiovascular events, with a focus on pneumolysin and macrolide antibiotics in pathogenesis and therapy. *Int. J. Mol. Sci.*, 24(13): 11038.
- Assimakopoulos, S.F., Aretha, D., Komninos, D., Dimitropoulou, D., Lagadinou, M., Leonidou, L., Oikonomou, I., Mouzaki, A., Marangos, M., 2021. N-acetyl-cysteine reduces the risk for mechanical ventilation and mortality in patients with COVID-19 pneumonia: a two-center retrospective cohort study. *Infect. Dis.*, 53(11): 847-854.
- Astasio-Picado, Á., Jiménez, F.J.P., López-Sánchez, M., Jurado-Palomo, J., Zabala-Baños, M.d.C., 2022. Pneumonia associated with mechanical ventilation: Management and preventive aspects. *Appl. Sci.*, 12(20): 10633.
- Badraoui, R., Alrashedi, M.M., El-May, M.V., Bardakci, F., 2021. Acute respiratory distress syndrome: a life threatening associated complication of SARS-CoV-2 infection inducing COVID-19. *J. Biomol. Struct. Dyn.*, 39(17): 6842-6851.
- Bai, L., Yang, L., Shi, X., Huang, W., 2022. Effect of PDCA circulation nursing intervention on prognosis of patients with severe pneumonia. *Am. J. Transl. Res.*, 14(1): 252.
- Battaglini, D., Iavarone, I.G., Robba, C., Ball, L., Silva, P.L., Rocco, P.R., 2023a. Mechanical ventilation in patients with acute respiratory distress syndrome: current status and future perspectives. *Expert Rev. Med. Devices.*, 20(11): 905-917.
- Battaglini, D., Parodi, L., Cinotti, R., Asehnoune, K., Taccone, F.S., Orengo, G., Zona, G., Uccelli, A., Ferro, G., Robba, M., 2023b. Ventilator-associated pneumonia in neurocritically ill patients: insights from the ENIO international prospective observational study. *Respir. Res.*, 24(1): 146.
- Battaglini, D., Sottano, M., Ball, L., Robba, C., Rocco, P.R., Pelosi, P., 2021. Ten golden rules for individualized mechanical ventilation in acute respiratory distress syndrome. *J. Intensive Care Med.*, 1(1): 42-51.
- Bonaventura, A., Vecchié, A., Dagna, L., Martinod, K., Dixon, D.L., Van Tassel, B.W., Dentali, F., Montecucco, F., Massberg, S., Levi, M., 2021. Endothelial dysfunction and immunothrombosis as key pathogenic mechanisms in COVID-19. *Nat. Rev. Immunol.*, 21(5): 319-329.
- Bordon, J., Akca, O., Furmanek, S., Cavallazzi, R.S., Suliman, S., Aboelnasr, A., Sinanova, B., Ramirez, J.A., 2021. Acute respiratory distress syndrome and time to weaning off the invasive mechanical ventilator among patients with COVID-19 pneumonia. *J. Clin. Med.*, 10(13): 2935.
- Broadhurst, A., Botha, C., Calligaro, G., Lee, C., Lalla, U., Koegelenberg, C., Gopalan, P., Joubert, I., Richards, G., Allwood, B., 2022. The optimal management of the patient with COVID-19 pneumonia: HFNC,

- NIV/CPAP or mechanical ventilation? *Afr. J. Thorac. Crit. Care Med.*, 28(3): 119-128.
- Calligaro, G.L., Lalla, U., Audley, G., Gina, P., Miller, M.G., Mendelson, M., Dlamini, S., Wasserman, S., Meintjes, G., Peter, J., 2020. The utility of high-flow nasal oxygen for severe COVID-19 pneumonia in a resource-constrained setting: A multi-centre prospective observational study. *EClinicalMed.*, 28.
- Chen, S., Qiu, X., Tan, X., Fang, Z., Jin, Y., 2022. A model-based hybrid soft actor-critic deep reinforcement learning algorithm for optimal ventilator settings. *Infor. Sci.*, 611: 47-64.
- Cilloniz, C., Pericas, J.M., Curioso, W.H., 2023. Interventions to improve outcomes in community-acquired pneumonia. *Expert Rev. Anti-infect. Ther.*, 21(10): 1071-1086.
- Clementi, N., Ghosh, S., De Santis, M., Castelli, M., Criscuolo, E., Zanoni, I., Clementi, M., Mancini, N., 2021. Viral respiratory pathogens and lung injury. *Clin. Microbiol. Rev.*, 34(3): 10.1128/cmr.00103-20.
- Coelho, L., Moniz, P., Guerreiro, G., Póvoa, P., 2023. Airway and respiratory devices in the prevention of ventilator-associated Pneumonia. *Med.*, 59(2): 199.
- Cui, Z., Ma, Y., Yu, Y., Li, N., Wang, J., Wang, A., Tan, Q., 2023. Short-term exposure to ambient fine particulate pollution aggravates ventilator-associated pneumonia in pediatric intensive care patients undergoing cardiovascular surgeries. *Environ. Health.*, 22(1): 39.
- D'Cruz, R.F., Kaltsakas, G., Suh, E.-S., Hart, N., 2023. Quality of life in patients with chronic respiratory failure on home mechanical ventilation. *Eur. Respir. Rev.*, 32(168).
- Deshpande, A., Klompas, M., Yu, P.-C., Imrey, P.B., Pallotta, A.M., Higgins, T., Haessler, S., Zilberberg, M.D., Lindenauer, P.K., Rothberg, M.B., 2022. Influenza testing and treatment among patients hospitalized with community-acquired pneumonia. *Chest.*, 162(3): 543-555.
- Diehl, J.-L., Peron, N., Chocron, R., Debuc, B., Guerot, E., Hauw-Berlemont, C., Hermann, B., Augy, J., Younan, R., Novara, A., 2020. Respiratory mechanics and gas exchanges in the early course of COVID-19 ARDS: a hypothesis-generating study. *Ann. Intensive Care.*, 10: 1-7.
- Dimbath, E., Maddipati, V., Stahl, J., Sewell, K., Domire, Z., George, S., Vahdati, A., 2021. Implications of microscale lung damage for COVID-19 pulmonary ventilation dynamics: A narrative review. *Life Sci.*, 274: 119341.
- Dogru, B.N., Kiliccalan, I., Asci, E.S., Peker, S.C., 2020. Blunt trauma related chest wall and pulmonary injuries: An overview. *Chin. J. Traumatol.*, 23(03): 125-138.
- Duggal, A., Scheraga, R., Sacha, G.L., Wang, X., Huang, S., Krishnan, S., Siuba, M.T., Torbic, H., Dugar, S., Mucha, S., 2024. Forecasting disease trajectories in critical illness: comparison of probabilistic dynamic systems to static models to predict patient status in the intensive care unit. *BMJ Open.*, 14(2): e079243.
- Dupuis, C., Bouadma, L., de Montmollin, E., Goldgran-Toledano, D., Schwebel, C., Reignier, J., Neuville, M., Ursino, M., Siami, S., Ruckly, S., 2021. Association between early invasive mechanical ventilation and day-60 mortality in acute hypoxemic respiratory failure related to coronavirus disease-2019 pneumonia. *Crit. Care Explor.*, 3(1): e0329.
- Ebrahimian, S., Homayounieh, F., Rockenbach, M.A., Putha, P., Raj, T., Dayan, I., Bizzo, B.C., Buch, V., Wu, D., Kim, K., 2021. Artificial intelligence matches subjective severity assessment of pneumonia for prediction of patient outcome and need for mechanical ventilation: a cohort study. *Sci. Rep.*, 11(1): 858.
- Ewers, M., Lehmann, Y., 2022. "The Devices Themselves Aren't the Problem"—Views of Patients and Their Relatives on Medical Technical Aid Supply in Home Mechanical Ventilation: An Explorative Qualitative Study, *Healthcare. MDPI*, pp. 1466.
- Fally, M., Haseeb, F., Kouta, A., Hansel, J., Robey, R.C., Williams, T., Welte, T., Felton, T., Mathioudakis, A.G., 2024. Unravelling the complexity of ventilator-associated pneumonia: a systematic methodological literature review of diagnostic criteria and definitions used in clinical research. *Crit. Care*, 28(1): 214.

- Fernando, S.M., Tran, A., Cheng, W., Klompas, M., Kyeremanteng, K., Mehta, S., English, S.W., Muscedere, J., Cook, D.J., Torres, A., 2020. Diagnosis of ventilator-associated pneumonia in critically ill adult patients—a systematic review and meta-analysis. *Intensive Care Med.*, 46: 1170-1179.
- Ferrer, M., De Pascale, G., Tanzarella, E.S., Antonelli, M., 2024. Severe Community-Acquired Pneumonia: Noninvasive Mechanical Ventilation, Intubation, and HFNT, *Seminars in Respiratory and Critical Care Medicine*. Thieme Medical Publishers, Inc., pp. 169-186.
- Fonseca, M., Summer, R., Roman, J., 2021. Acute exacerbation of interstitial lung disease as a sequela of COVID-19 pneumonia. *Am. J. Med. Sci.*, 361(1): 126-129.
- Garnier, M., Constantin, J.-M., Heming, N., Camous, L., Ferré, A., Razazi, K., Lapidus, N., Investigators, C.-I., 2023. Epidemiology, risk factors and prognosis of ventilator-associated pneumonia during severe COVID-19: Multicenter observational study across 149 European Intensive Care Units. *Anaesth. Crit. Care Pain Med.*, 42(1): 101184.
- Georgakopoulou, V.E., Gkoufa, A., Aravantinou-Fatorou, A., Trakas, I., Trakas, N., Faropoulos, K., Paterakis, K., Fotakopoulos, G., 2023. Lower respiratory tract infections due to multi-drug resistant pathogens in central nervous system injuries. *Biomed. Rep.*, 18(4): 30.
- Goligher, E.C., Jonkman, A.H., Dianti, J., Vaporidi, K., Beitler, J.R., Patel, B.K., Yoshida, T., Jaber, S., Dres, M., Mauri, T., 2020. Clinical strategies for implementing lung and diaphragm-protective ventilation: avoiding insufficient and excessive effort. *Intensive Care Med.*, 46(12): 2314-2326.
- Gosangi, B., Rubinowitz, A.N., Irugu, D., Gange, C., Bader, A., Cortopassi, I., 2022. COVID-19 ARDS: a review of imaging features and overview of mechanical ventilation and its complications. *Emerg. Radiol.*: 1-12.
- Gragueb-Chatti, I., Lopez, A., Hamidi, D., Guervilly, C., Loundou, A., Daviet, F., Cassir, N., Papazian, L., Forel, J.-M., Leone, M., 2021. Impact of dexamethasone on the incidence of ventilator-associated pneumonia and blood stream infections in COVID-19 patients requiring invasive mechanical ventilation: a multicenter retrospective study. *Ann. Intensive Care.*, 11(1): 87.
- Grasselli, G., Cattaneo, E., Florio, G., Ippolito, M., Zanella, A., Cortegiani, A., Huang, J., Pesenti, A., Einav, S., 2021. Mechanical ventilation parameters in critically ill COVID-19 patients: a scoping review. *Crit. Care.*, 25: 1-11.
- Guidet, B., Vallet, H., Flaatten, H., Joynt, G., Bagshaw, S.M., Leaver, S.K., Beil, M., Du, B., Forte, D.N., Angus, D.C., 2024. The trajectory of very old critically ill patients. *Intensive Care Med.*, 50(2): 181-194.
- Gupta, B., Jain, G., Chandrakar, S., Gupta, N., Agarwal, A., 2021. Arterial blood gas as a predictor of mortality in COVID pneumonia patients initiated on noninvasive mechanical ventilation: a retrospective analysis. *Indian J. Crit. Care Med.*, 25(8): 866.
- Güven, B.B., Ertürk, T., Kompe, Ö., Ersoy, A., 2021. Serious complications in COVID-19 ARDS cases: pneumothorax, pneumomediastinum, subcutaneous emphysema and haemothorax. *Epidemiol. Infect.*, 149: e137.
- Hassan, A., Lai, W., Alison, J., Huang, S., Milross, M., 2021. Effect of intrapulmonary percussive ventilation on intensive care unit length of stay, the incidence of pneumonia and gas exchange in critically ill patients: a systematic review. *PloS One.*, 16(7): e0255005.
- Hess, D.R., Kallet, R.H., Beitler, J.R., 2020. Ventilator sharing: the good, the bad, and the ugly. *Daedalus Enterprises Inc.*, pp. 1059-1062.
- Hou, K., Wu, Z.-X., Chen, X.-Y., Wang, J.-Q., Zhang, D., Xiao, C., Zhu, D., Koya, J.B., Wei, L., Li, J., 2022. Microbiota in health and diseases. *Signal Transduct. Target. Ther.*, 7(1): 135.
- Howroyd, F., Chacko, C., MacDuff, A., Gautam, N., Pouchet, B., Tunnicliffe, B., Weblin, J., Gao-Smith, F., Ahmed, Z., Duggal, N.A.,

2024. Ventilator-associated pneumonia: pathobiological heterogeneity and diagnostic challenges. *Nat. Commun.*, 15(1): 6447.
- Huang, H.-Y., Huang, C.-Y., Li, L.-F., 2022. Prolonged mechanical ventilation: outcomes and management. *J. Clin. Med.*, 11(9): 2451.
- Hughes, N., Jia, Y., Sujan, M., Lawton, T., Habli, I., McDermid, J., 2024. Contextual design requirements for decision-support tools involved in weaning patients from mechanical ventilation in intensive care units. *Appl. Ergon.*, 118: 104275.
- Hurry, B., 2024. Managing ARDS in COVID-19: Optimal Mechanical Ventilation Duration and Clinical Implications.
- Investigators, S.S.G., Maia, I.S., Medrado Jr, F.A., Tramujas, L., Tomazini, B.M., Oliveira, J.S., Sady, E.R.R., Barbante, L.G., Nicola, M.L., Gurgel, R.M., 2024. Prospective, randomized, controlled trial assessing the effects of a driving pressure-limiting strategy for patients with acute respiratory distress syndrome due to community-acquired pneumonia (STAMINA trial): protocol and statistical analysis plan. *Critical Care Sci.*, 36: e20240210en.
- Iqbal, M.N., 2021. Smog and Respiratory Infections: Continuing Challenges. *Int. J. Nanotechnol. Allied Sci.*, 5(2): 34-36.
- Izumi, M., Akifusa, S., 2021. Tongue cleaning in the elderly and its role in the respiratory and swallowing functions: Benefits and medical perspectives. *J. Oral. Rehabil.*, 48(12): 1395-1403.
- Janssens, J.-P., Michel, F., Schwarz, E.I., Prella, M., Bloch, K., Adler, D., Brill, A.-K., Geenens, A., Karrer, W., Ognà, A., 2021. Long-term mechanical ventilation: recommendations of the Swiss Society of Pulmonology. *Respir.*, 99(10): 867-902.
- Johnstone, J., Meade, M., Lauzier, F., Marshall, J., Duan, E., Dionne, J., Arabi, Y.M., Heels-Ansdell, D., Thabane, L., Lamarche, D., 2021. Effect of probiotics on incident ventilator-associated pneumonia in critically ill patients: a randomized clinical trial. *JAMA.*, 326(11): 1024-1033.
- Jones, B.E., Herman, D.D., Dela Cruz, C.S., Waterer, G.W., Metlay, J.P., Ruminjo, J.K., Thomson, C.C., 2020. Summary for clinicians: clinical practice guideline for the diagnosis and treatment of community-acquired pneumonia. *Ann. Am. Thorac. Soc.*, 17(2): 133-138.
- Karunarathna, I., Alvis, K., Gunasena, P., Hapuarachchi, T., Ekanayake, U., Rajapaksha, S., Gunawardana, K., Aluthge, P., Gunathilake, S., Bandara, S., Jayawardana, A., 2024a. Challenges and Solutions in Anesthesia for COPD Patients: A Perioperative Perspective, pp. 179-182.
- Karunarathna, I., De Alvis, K., Gunasena, P., Jayawardana, A., 2024b. Perioperative and ICU care for COPD patients: Enhancing outcomes through multidisciplinary approaches. ResearchGate. <https://www.researchgate.net/publication/383024887>.
- Karunarathna, I., Gunawardana, K., Aluthge, P., Jayawardana, A., 2024c. Innovative therapies and future directions in pulmonary hemorrhage management. ResearchGate. <https://www.researchgate.net/publication/383526615>.
- Karunarathna, I., Kusumarathna, K., Jayathilaka, P., Rathnayake, B., Gunathilake, S., Senarathna, R., Wijayawardana, K., Priyalath, N., Gunarathna, I., Walgama, K., 2024d. Understanding Ventilator-Associated Pneumonia: Causes, Prevention, and Management. Uva Clinical Lab. Retrieved from ResearchGate.
- Kepekci, A., 2020. Ventilator-associated pneumonia rates and distribution of causative microorganisms in the second stage intensive care unit. *Med.*, 9(3): 635-9.
- Kim, M.W., Yu, S.H., Yang, U., Nukiwa, R., Cho, H.J., Kwon, N.S., Yong, M.J., Kim, N.H., Lee, S.H., Lee, J.H., 2024. Alveolar microdynamics during tidal ventilation in live animals imaged by SPring-8 synchrotron. *Adv. Sci.*, 11(33): 2306256.
- Kosutova, P., Mikolka, P., 2021. Aspiration syndromes and associated lung injury: incidence, pathophysiology and

- management. *Physiol. Res.*, 70(Suppl 4): S567.
- Kózka, M., Sega, A., Wojnar-Gruszka, K., Tarnawska, A., Gniadek, A., 2020. Risk factors of pneumonia associated with mechanical ventilation. *Int. J. Environ. Res. Public Health.*, 17(2): 656.
- Kumar, V., 2020. Pulmonary innate immune response determines the outcome of inflammation during pneumonia and sepsis-associated acute lung injury. *Front. Immunol.*, 11: 1722.
- Land, W.G., 2021. Role of DAMPs in respiratory virus-induced acute respiratory distress syndrome—with a preliminary reference to SARS-CoV-2 pneumonia. *Genes. Immun.*, 22(3): 141-160.
- Lara, P.C., Burgos, J., Macias, D., 2020. Low dose lung radiotherapy for COVID-19 pneumonia. The rationale for a cost-effective anti-inflammatory treatment. *Clin. Transl. Radiat. Oncol.*, 23: 27-29.
- Lehingue, S., Allardet-Servent, J., Ferdani, A., Hraich, S., Forel, J.-M., Arnal, J.-M., Prud'homme, E., Penaranda, G., Bourenne, J., Monnet, O., 2022. Physiologic effects of the awake prone position combined with high-flow nasal oxygen on gas exchange and work of breathing in patients with severe COVID-19 pneumonia: a randomized crossover trial. *Critical Care Explor.*, 4(12): e0805.
- Li, Y., Liu, C., Xiao, W., Song, T., Wang, S., 2020. Incidence, risk factors, and outcomes of ventilator-associated pneumonia in traumatic brain injury: a meta-analysis. *Neurocrit. Care.*, 32(1): 272-285.
- Liaqat, A., Mason, M., Foster, B.J., Kulkarni, S., Barlas, A., Farooq, A.M., Patak, P., Liaqat, H., Basso, R.G., Zaman, M.S., 2022. Evidence-based mechanical ventilatory strategies in ARDS. *J. Clin. Med.*, 11(2): 319.
- Lima, W.G., Brito, J.C.M., da Cruz Nizer, W.S., 2020. Ventilator-associated pneumonia (VAP) caused by carbapenem-resistant *Acinetobacter baumannii* in patients with COVID-19: Two problems, one solution? *Med. Hypotheses.*, 144: 110139.
- Liu, X., Wang, L., 2022. Comparison of the effects of different mechanical ventilation modes on the incidence of ventilation-associated pneumonia: a case study of patients undergoing thoracic surgery. *Am. J. Transl. Res.*, 14(12): 8668.
- Liu, Y., Sun, T., Cai, Y., Zhai, T., Huang, L., Zhang, Q., Wang, C., Chen, H., Huang, X., Li, M., 2023. Clinical characteristics and prognosis of pneumonia-related bloodstream infections in the intensive care unit: a single-center retrospective study. *Front. Public Health.*, 11: 1249695.
- Liu, Y., Wang, Q., Hu, J., Zhou, F., Liu, C., Li, J., Fu, Y., Dang, H., 2022. Characteristics and risk factors of children requiring prolonged mechanical ventilation vs. non-prolonged mechanical ventilation in the PICU: a prospective single-center study. *Front. Pediatr.*, 10: 830075.
- Llitjos, J.-F., Bredin, S., Lascarrou, J.-B., Soumagne, T., Cojocaru, M., Leclerc, M., Lepetit, A., Gouhier, A., Charpentier, J., Piton, G., 2021. Increased susceptibility to intensive care unit-acquired pneumonia in severe COVID-19 patients: a multicentre retrospective cohort study. *Ann. Intensive Care.*, 11: 1-8.
- Lodhia, J., Eyre, L., Smith, M., Toth, L., Troxler, M., Milton, R., 2023. Management of thoracic trauma. *Anaesth.*, 78(2): 225-235.
- Long, M.E., Mallampalli, R.K., Horowitz, J.C., 2022. Pathogenesis of pneumonia and acute lung injury. *Clin. Sci.*, 136(10): 747-769.
- Longhitano, Y., Zanza, C., Romenskaya, T., Saviano, A., Persiano, T., Leo, M., Piccioni, A., Betti, M., Maconi, A., Pindinello, I., 2021. Single-breath counting test predicts non-invasive respiratory support requirements in patients with COVID-19 pneumonia. *J. Clin. Med.*, 11(1): 179.
- Luo, W., Xing, R., Wang, C., 2021. The effect of ventilator-associated pneumonia on the prognosis of intensive care unit patients within 90 days and 180 days. *BMC Infect. Dis.*, 21: 1-7.
- Luque-Paz, D., Tattevin, P., Jaubert, P., Reizine, F., Kouatchet, A., Camus, C., 2021. Selective digestive decontamination to

- reduce the high rate of ventilator-associated pneumonia in critical COVID-19. *Anaesth. Crit. Care Pain Med.*, 41(1): 100987.
- Luyt, C.-E., Bouadma, L., Morris, A.C., Dhanani, J.A., Kollef, M., Lipman, J., Martin-Loeches, I., Nseir, S., Ranzani, O.T., Roquilly, A., 2020. Pulmonary infections complicating ARDS. *Intensive Care Med.*, 46: 2168-2183.
- MacLeod, M., Papi, A., Contoli, M., Beghé, B., Celli, B.R., Wedzicha, J.A., Fabbri, L.M., 2021. Chronic obstructive pulmonary disease exacerbation fundamentals: diagnosis, treatment, prevention and disease impact. *Respirol.*, 26(6): 532-551.
- Mah, A.J., Nguyen, T., Ghazi Zadeh, L., Shadgan, A., Khaksari, K., Nourizadeh, M., Zaidi, A., Park, S., Gandjbakhche, A.H., Shadgan, B., 2022. Optical Monitoring of breathing patterns and tissue oxygenation: A potential application in COVID-19 screening and monitoring. *Sens.*, 22(19): 7274.
- Manickavel, S., 2021. Pathophysiology of respiratory failure and physiology of gas exchange during ECMO. In: *J. Thorac. Cardiovasc. Surg.*, 37: 203-209.
- Marietta, M., Vandelli, P., Mighali, P., Vicini, R., Coluccio, V., D'Amico, R., Silva, C.-H.S.G.D.A.L.B.E.C.M.C.D.I.A.M.M.C.M.S.O.G.P.A.P.L.S.M., 2020. Randomised controlled trial comparing efficacy and safety of high versus low Low-Molecular Weight Heparin dosages in hospitalized patients with severe COVID-19 pneumonia and coagulopathy not requiring invasive mechanical ventilation (COVID-19 HD): a structured summary of a study protocol. *Trials*, 21: 1-5.
- Martin-Loeches, I., Reyes, L.F., Nseir, S., Ranzani, O., Pova, P., Diaz, E., Schultz, M.J., Rodríguez, A.H., Serrano-Mayorga, C.C., De Pascale, G., 2023a. European Network for ICU-Related Respiratory Infections (ENIRRI): a multinational, prospective, cohort study of nosocomial LRTI. *Intensive Care Med.*, 49(10): 1212-1222.
- Martin-Loeches, I., Torres, A., Nagavci, B., Aliberti, S., Antonelli, M., Bassetti, M., Bos, L., Chalmers, J.D., Derde, L., de Waele, J., Garnacho-Montero, J., Kollef, M., Luna, C., Menendez, R., Niederman, M., Ponomarev, D., Restrepo, M., Rigau, D., Schultz, M.J., Weiss, E., Welte, T., Wunderink, R., 2023b. ERS/ESICM/ESCMID/ALAT guidelines for the management of severe community-acquired pneumonia. *Eur. Respir. J.*, 61(4).
- Mason, R.J., 2020. Thoughts on the alveolar phase of COVID-19. *Am. J. Physiol. Lung Cell. Mol. Physiol.*, 319(1): L115-L120.
- McGuinness, G., Zhan, C., Rosenberg, N., Azour, L., Wickstrom, M., Mason, D.M., Thomas, K.M., Moore, W.H., 2020. Increased incidence of barotrauma in patients with COVID-19 on invasive mechanical ventilation. *Radiol.*, 297(2): E252-E262.
- Meawed, T.E., Ahmed, S.M., Mowafy, S.M., Samir, G.M., Anis, R.H., 2021. Bacterial and fungal ventilator associated pneumonia in critically ill COVID-19 patients during the second wave. *J. Infect. Public Health.*, 14(10): 1375-1380.
- Megahed, M.M., El-Menshaw, A.M., Ibrahim, A.M., 2021. Use of early bronchoscopy in mechanically ventilated patients with aspiration pneumonitis. *Indian J. Crit. Care Med.*, 25(2): 146.
- Mondeshki, T., Bilyukov, R., Tomov, T., Mihaylov, M., Mitev, V., Mondeshki, T.L., Bilyukov, R., 2022. Complete, rapid resolution of severe bilateral pneumonia and acute respiratory distress syndrome in a COVID-19 patient: Role for a unique therapeutic combination of inhalations with bromhexine, higher doses of colchicine, and hymecromone. *Cureus.*, 14(10).
- Motes, A., Singh, T., Vinan Vega, N., Nugent, K., 2023. A focused review of the initial management of patients with acute respiratory distress syndrome. *J. Clin. Med.*, 12(14): 4650.
- Mudhar, O., Goswami, S.K., DeMellow, J., 2022. Incidence of barotrauma in COVID-19 patients requiring mechanical ventilation: a retrospective study in a community hospital. *Cureus.*, 14(10).

- Nair, G.B., Niederman, M.S., 2021. Updates on community acquired pneumonia management in the ICU. *Pharm. Ther.*, 217: 107663.
- Nascimento-Carvalho, C.M., 2020. Community-acquired pneumonia among children: the latest evidence for an updated management. *J. Pediatr.*, 96: 29-38.
- Navarra, S.M., Congedo, M.T., Pennisi, M.A., 2020. Indications for non-invasive ventilation in respiratory failure. *Rev. Recent Clin. Trials.*, 15(4): 251-257.
- Nolley, E.P., Sahetya, S.K., Hochberg, C.H., Hossen, S., Hager, D.N., Brower, R.G., Stuart, E.A., Checkley, W., 2023. Outcomes among mechanically ventilated patients with severe pneumonia and acute hypoxemic respiratory failure from SARS-CoV-2 and other etiologies. *JAMA Netw. Open.*, 6(1): e2250401-e2250401.
- Núñez-Fernández, M., Ramos-Hernández, C., García-Río, F., Torres-Durán, M., Nodar-Germiñas, A., Tilve-Gómez, A., Rodríguez-Fernández, P., Valverde-Pérez, D., Ruano-Raviña, A., Fernández-Villar, A., 2021. Alterations in respiratory function test three months after hospitalisation for COVID-19 pneumonia: value of determining nitric oxide diffusion. *J. Clin. Med.*, 10(10): 2119.
- Núñez, S.A., Roveda, G., Zárate, M.S., Emmerich, M., Verón, M.T., 2021. Ventilator-associated pneumonia in patients on prolonged mechanical ventilation: description, risk factors for mortality, and performance of the SOFA score. *J. Bras. Pneumol.*, 47: e20200569.
- Omwenga, C., 2020. Pattern of bacterial colonization and antimicrobial susceptibility of tracheal aspirates in tracheostomised patients at the Kenyatta National Hospital, University of Nairobi.
- Pagliano, P., Sellitto, C., Conti, V., Ascione, T., Esposito, S., 2021. Characteristics of viral pneumonia in the COVID-19 era: an update. *Infect.*, 49(4): 607-616.
- Papazian, L., Klompas, M., Luyt, C.-E., 2020. Ventilator-associated pneumonia in adults: a narrative review. *Intensive Care Med.*, 46(5): 888-906.
- Patil, S., Toshniwal, S., Acharya, A., Narwade, G., 2022. Role of "Ferritin" in COVID-19 pneumonia: Sensitive marker of inflammation, predictor of mechanical ventilation, and early marker of post-COVID-lung fibrosis—A prospective, observational, and interventional study in a tertiary care setting in India. *Muller. J. Med. Sci. Res.*, 13(1): 28-34.
- Pawlik, J., Tomaszek, L., Mazurek, H., Mędrzycka-Dąbrowska, W., 2022. Risk Factors and Protective Factors against Ventilator-Associated Pneumonia—A Single-Center Mixed Prospective and Retrospective Cohort Study. *J. Pers. Med.*, 12(4): 597.
- Pelosi, P., Tonelli, R., Torregiani, C., Baratella, E., Confalonieri, M., Battaglini, D., Marchioni, A., Confalonieri, P., Cini, E., Salton, F., 2022. Different methods to improve the monitoring of noninvasive respiratory support of patients with severe pneumonia/ARDS due to COVID-19: an update. *J. Clin. Med.*, 11(6): 1704.
- Peña-López, Y., Campins-Martí, M., Slöcker-Barrio, M., Bustinza, A., Alejandre, C., Jordán-García, I., Ortiz-Álvarez, A., López-Castilla, J.D., Pérez, E., Schüffelmann, C., 2022. Ventilator-associated events in children: a multicentre prospective cohort study. *Anaesth. Crit. Care Pain Med.*, 41(3): 101072.
- Peña-López, Y., Slocker-Barrio, M., de-Carlos-Vicente, J.-C., Serrano-Megías, M., Jordán-García, I., Rello, J., Abril-Molina, A., Alejandre, C., Arjona, D., Bustinza, A., 2024. Outcomes associated with ventilator-associated events (VAE), respiratory infections (VARI), pneumonia (VAP) and tracheobronchitis (VAT) in ventilated pediatric ICU patients: A multicentre prospective cohort study. *Intensive Crit. Care Nurs.*, 83: 103664.
- Peng, Q.-Y., Wang, X.-T., Zhang, L.-N., Group, C.C.C.U.S., 2020. Using echocardiography to guide the treatment of novel coronavirus pneumonia. Springer, pp. 1-3.
- Pickens, C.O., Gao, C.A., Cuttica, M.J., Smith, S.B., Pesce, L.L., Grant, R.A., Kang, M., Morales-Nebreda, L., Bavishi, A.A., 97

- Arnold, J.M., 2021. Bacterial superinfection pneumonia in patients mechanically ventilated for COVID-19 pneumonia. *Am. J. Respir. Crit. Care Med.*, 204(8): 921-932.
- Qureshi, S.M., Mustafa, R., 2018. Measurement of respiratory function: gas exchange and its clinical applications. *Anaesth. Intensive Care Med.*, 19(2): 65-71.
- Rackley, C.R., 2020. Monitoring during mechanical ventilation. *Respir. Care.*, 65(6): 832-846.
- Rajdev, K., Spanel, A.J., McMillan, S., Lahan, S., Boer, B., Birge, J., Thi, M., 2021. Pulmonary barotrauma in COVID-19 patients with ARDS on invasive and non-invasive positive pressure ventilation. *J. Intensive Care Med.*, 36(9): 1013-1017.
- Ramirez-Estrada, S., Peña-Lopez, Y., Viecei, T., Rello, J., 2023. Ventilator-associated events: from surveillance to optimizing management. *J. Intensive Med.*, 3(03): 204-211.
- Rejas, J., Sicras-Mainar, A., Sicras-Navarro, A., Lwoff, N., Méndez, C., 2022. All-cause community acquired pneumonia cost by age and risk in real-world conditions of care in Spain. *Expert Rev. Pharmacoecon. Outcomes Res.*, 22(5): 853-867.
- Reynolds, J.M., Guidry-Grimes, L., Savin, K., 2021. Against personal ventilator reallocation. *Camb. Q. Healthc. Ethics.*, 30(2): 272-284.
- Rosenthal, V.D., Jin, Z., Memish, Z.A., Rodrigues, C., Myatra, S.N., Kharbanda, M., Valderrama-Beltran, S.L., Mehta, Y., Daboor, M.A., Todi, S.K., 2023. Multinational prospective cohort study of rates and risk factors for ventilator-associated pneumonia over 24 years in 42 countries of Asia, Africa, Eastern Europe, Latin America, and the Middle East: Findings of the International Nosocomial Infection Control Consortium (INICC). *Antimicrob. Steward. Healthc. Epidemiol.*, 3(1): e6.
- Sánchez-Guijo, F., García-Arranz, M., López-Parra, M., Monedero, P., Mata-Martínez, C., Santos, A., Sagredo, V., Álvarez-Avello, J.-M., Guerrero, J.E., Pérez-Calvo, C., 2020. Adipose-derived mesenchymal stromal cells for the treatment of patients with severe SARS-CoV-2 pneumonia requiring mechanical ventilation. A proof of concept study. *EClinicalMedicine.*, 25.
- Savary, D., Drennan, I.R., Badat, B., Grieco, D.L., Piraino, T., Lesimple, A., Charbonney, E., Fritz, C., Delisle, S., Ouellet, P., Mercat, A., Bronchti, G., Brochard, L., Richard, J.C., 2020. Gastric insufflation during cardiopulmonary resuscitation: A study in human cadavers. *Resuscitation.*, 146: 111-117.
- See, X.Y., Wang, T.H., Chang, Y.-C., Lo, J., Liu, W., Choo, C.Y.W., Lee, Y.-C., Ma, K.S.K., Chiang, C.-H., Hsia, Y.P., 2024. Impact of different corticosteroids on severe community-acquired pneumonia: a systematic review and meta-analysis. *BMJ Open Respir. Res.*, 11(1).
- Shah, H., Ali, A., Patel, A.A., Abbagoni, V., Goswami, R., Kumar, A., Botero, F.V., Otite, E., Tomar, H., Desai, M., 2022. Trends and factors associated with ventilator-associated pneumonia: a national perspective. *Cureus.*, 14(3).
- Sharma, A.K., Sharma, V., Sharma, A., Pallikkuth, S., Sharma, A.K., 2021. Current paradigms in COVID-19 research: proposed treatment strategies, recent trends and future directions. *Curr. Med. Chem.*, 28(16): 3173-3192.
- Sriram, K., Insel, M.B., Insel, P.A., 2021. Inhaled β_2 adrenergic agonists and other cAMP-elevating agents: therapeutics for alveolar injury and acute respiratory disease syndrome? *Pharmacol. Rev.*, 73(4): 1659-1697.
- Stainer, A., Faverio, P., Busnelli, S., Catalano, M., Della Zoppa, M., Marruchella, A., Pesci, A., Luppi, F., 2021. Molecular biomarkers in idiopathic pulmonary fibrosis: state of the art and future directions. *Int. J. Mol. Sci.*, 22(12): 6255.
- Stotts, C., Corrales-Medina, V.F., Rayner, K.J., 2023. Pneumonia-induced inflammation, resolution and cardiovascular disease: causes, consequences and clinical opportunities. *Circ. Res.*, 132(6): 751-774.
- Strathdee, S.A., Hatfull, G.F., Mutalik, V.K., Schooley, R.T., 2023. Phage therapy:

- From biological mechanisms to future directions. *Cell.*, 186(1): 17-31.
- Szarpak, L., Wisco, J., Boyer, R., 2021. How healthcare must respond to ventilator-associated pneumonia (VAP) in invasively mechanically ventilated COVID-19 patients. *Am. J. Emerg. Med.*, 48: 361.
- Taha, I., Abdou, Y., Hammad, I., Nady, O., Hassan, G., Farid, M.F., Alofi, F.S., Alharbi, N., Salamah, E., Aldeeb, N., 2022. Utilization of Antibiotics for Hospitalized Patients with Severe Coronavirus Disease 2019 in Al-Madinah Al-Munawara, Saudi Arabia: A Retrospective Study. *Infect. Drug Resist.*, 7401-7411.
- Takahashi, T., Saito, A., Kuronuma, K., Nishikiori, H., Chiba, H., 2022. *Pneumocystis jirovecii* pneumonia associated with COVID-19 in patients with interstitial pneumonia. *Med.*, 58(9): 1151.
- Tang, J., Gong, L., Xiong, T., Chen, C., Tian, K., Wang, A., Huang, Y., Liu, W., Zhou, R., Zhu, J., 2023. Volume-targeted ventilation vs pressure-controlled ventilation for very low birthweight infants: a protocol of a randomized controlled trial. *Trials.*, 24(1): 536.
- Teo, Y.X., Geetha, H.S., Mishra, A.K., Lal, A., 2023. Pneumomediastinum and pneumothorax in acute respiratory distress syndrome (ARDS) patients: a narrative review. *Mediastinum*, 8: 3.
- Thibeault, C., Suttrop, N., Opitz, B., 2021. The microbiota in pneumonia: from protection to predisposition. *Sci. Transl. Med.*, 13(576): eaba0501.
- Thomas, R.E., Erickson, S., Hullett, B., Minutillo, C., Lethbridge, M., Vijayasekaran, S., Agrawal, S., Bulsara, M.K., Rao, S.C., 2021. Comparison of the efficacy and safety of cuffed versus uncuffed endotracheal tubes for infants in the intensive care setting: a pilot, unblinded RCT. *Arch. Dis. Child. Fetal Neonatal Ed.*, 106(6): 614-620.
- Tillotson, G., Lodise, T., Classi, P., Mildvan, D., McKinnell, J.A., 2020. Antibiotic treatment failure and associated outcomes among adult patients with community-acquired pneumonia in the outpatient setting: a real-world US insurance claims database study. *Open Forum Infectious Diseases*. Oxford University Press US, pp. ofaa065.
- Toth, A., Steinmeyer, S., Kannan, P., Gray, J., Jackson, C.M., Mukherjee, S., Demmert, M., Sheak, J.R., Benson, D., Kitzmiller, J., 2022. Inflammatory blockade prevents injury to the developing pulmonary gas exchange surface in preterm primates. *Sci. Transl. Med.*, 14(638): eabl8574.
- Tuyambaze, A., Hakizimana, C., 2023. Prevalence and risk factor associated with nosocomial infection among pediatric patients attending kibogora level two teaching hospital case study: Kibigora level two teaching hospital., Kibogora Polytechnic.
- Umemura, Y., Mitsuyama, Y., Minami, K., Nishida, T., Watanabe, A., Okada, N., Yamakawa, K., Nochioka, K., Fujimi, S., 2021. Efficacy and safety of nintedanib for pulmonary fibrosis in severe pneumonia induced by COVID-19: An interventional study. *Int. J. Infect. Dis.*, 108: 454-460.
- Waterer, G., 2021. What is pneumonia? *Breathe*, 17(3).
- Windisch, W., Weber-Carstens, S., Kluge, S., Rossaint, R., Welte, T., Karagiannidis, C., 2020. Invasive and non-invasive ventilation in patients with COVID-19. *Dtsch. Arztebl. Int.*, 117(31-32): 528.
- Wong, M., Bharadwaj, S., Lankford, A., Galey, J., Kodali, B., 2022. Mechanical ventilation and prone positioning in pregnant patients with severe COVID-19 pneumonia: experience at a quaternary referral center. *Int. J. Obstet. Anesth.*, 49: 103236.
- Yang, Q.-F., Shu, C.-M., 2024. Severe community-acquired pneumonia caused by *Chlamydia abortus* in China: a case report. *Front. Med.*, 11: 1426577.
- Zeng, C., Lagier, D., Lee, J.-W., Melo, M.F.V., 2022. Perioperative pulmonary atelectasis—part I: biology and mechanisms. *Anesthesiol.*, 136(1): 181.
- Ziaka, M., Exadaktylos, A., 2021. Brain–lung interactions and mechanical ventilation in patients with isolated brain injury. *Crit. Care.*, 25(1): 358.

