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Correlation between Mechanical Ventilation and Covid-19 Mortality

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Abstract
Background:*It is estimated that 20% of patients diagnosed with COVID-19 develop the severe form of the disease and may acquire acute respiratory distress syndrome, the most severe complication. From this, the patient ends up manifesting an acute hypoxemic respiratory failure and about 42 to 100% of these patients need respiratory assistance. The use of ventilators promotes better gas exchange performance and reduces the work of breathing, which can be non-invasive, through an external interface such as a face mask, or invasive, through intubation or tracheostomy, and only one in three patients with the new coronavirus who were admitted to these structures and intubated were actually able to recover and return home.*
Methods:*The work consists of exploratory bibliographical research in a documentary, statistical and retrospective field through the collection, comparison and correlation of data, including data on mechanical ventilation published in indexed journals where qualified and quantified data on ventilatory mechanics of patients with COVID-19, relating the ventilation mode and modality, the parameters used and the outcome (discharge or death) of the patients included in the research for data analysis and treatment.*
ResultsandConclusion:*This review showed that there may be a correlation between the ventilatory modality and parameters used in conducting mechanical ventilation with a higher or lower mortality rate, especially in relation to PEEP titration and driving pressure, highlighting the need for new evidence-based ventilatory guidelines.*
Keywords: *MechanicalVentilation, COVID-19, Mortality.*

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I. Introduction

After the first confirmed case of COVID-19 in Wuhan, capital of China's Hubei province in late 2019, cases were reported worldwide, on March 11, 2020 it was considered a pandemic according to WHO (2020), to date, there are more than 118 million confirmed cases and more than 2 million deaths worldwide.

In Brazil, the number of cases is equivalent to more than 11,202,305 and the number of deaths exceeds 270,656, according to data from the Ministry of Health extracted from the website www.gov.br/saude/pt-br/coronavirus, the moving average of new cases of covid-19 since the beginning of the year 2021 has risen 21% two weeks after Carnival, in March alone the country has been setting a record of death day after day. Three out of every ten people who went through the ICU with covid-19 died in Brazil, according to estimates by the platform of the Brazilian Association of Intensive Medicine (AMIB) which monitors 13,695 beds of this type, about a third of the country's total. According to the AMIB (2020), mortality is even higher in the group of patients who needed mechanical ventilation, according to the same platform, only one in three patients with the new coronavirus who were hospitalized in these structures and intubated actually managed to recover and return home.

Mechanical ventilators are one of the last resources for patients with severe respiratory failure after infection by the new coronavirus, this device is intended to replace the spontaneous breathing of these patients with artificial respiration (ANESI, 2019).

It is estimated that 20% of patients diagnosed with COVID-19 develop the severe form of the disease and may acquire acute respiratory distress syndrome (SARS), the most severe complication. From this, the patient ends up manifesting an acute hypoxemic respiratory failure and about 42 to 100% of these patients need respiratory assistance (ANESI, 2019). The use of ventilators promotes better gas exchange performance and reduces the work of breathing, which can be non-invasive, through an external interface such as a face mask, or invasive, through intubation or tracheostomy (HYZY & MCSPARRON, 2020).

COVID-19 is a viral infection of the airways that mainly affects epithelial/alveolar and endothelial cells, resulting in desquamation of pneumocytes, presence of hyaline membrane, formation and interstitial inflammation with lymphocyte infiltration. It is noteworthy that viral alterations also include multi-nucleated cells, syncytial cells and atypical pneumocytes in the interalveolar spaces that trigger SARS (MENDES et al. 2019). SARS causes fluid exudation, rich in plasma cells and proteins, causing an increase in permeability between the alveoli and capillaries that cover them. This process induces a local inflammatory response with the presence of leukocytes, platelets and fibrin which contributes to the formation of hyaline membrane and subsequent alveolar fibrosis, thus SARS results from an intense acute inflammatory response in the alveoli, preventing the physiological gas exchange of oxygen and carbon dioxide (WHYTE, 2020)

Based on an analysis of single cell RNA sequencing datasets derived from major human physiological systems, organs considered most vulnerable to SARS-CoV-2 infection due to their ACE2 expression levels include the lungs, the heart , the esophagus, the kidneys, the bladder and the ileum. This may explain the extrapulmonary manifestations associated with the infection. A lower expression of ACE2 in the nasal epithelium of children aged < 10 years compared to adults may explain why COVID-19 is less prevalent in children, however, further research on this is needed. According to Alcântara (2020) in COVID-19, MV decisions need to be guided depending on the pulmonary impairment, which can be mild, severe or critical. Thus, decisions in MV should be made considering the severity of the case and the profile of the phenotypes of patients with COVID-19.

The H phenotype represents patients with high lung elastance and good response to high PEEP levels, a presentation quite similar to Acute respiratory distress syndrome (ARDS), on the other hand, the L phenotype is characterized by low elastance and little or no response to PEEP in alveolar recruitment (ALHAZZANI W, 2020).

A comparison of mechanical ventilation protocols recommended by the Brazilian Associations of Cardiorespiratory Physiotherapy and Intensive Care Physiotherapy (ASSOBRAFIR), Brazilian Association of Intensive Medicine (AMIB) and Hospital Israelita Albert Einstein was performed.

ASSOBRAFIR uses the ventilatory pattern VCV or PCV, VC (tidal volume): 6ml/kg, PALTO PRESSURE: less than or equal to 30 cmH2O, DRIVING PRESSURE: -15 cmH2O, PEEP: Carry out individualized decremental PEEP adjustment, aiming at the lowest drivingpressure.PaCO²: ≥ 60 mmHg. AAMIB uses the ventilatory pattern VCV or PCV, VC: 6ml/kg, PALTÔ PRESSURE: <30cmH2O, DRIVING PRESSURE: - 15 cmH2O, the ideal PEEP setting remains not fully elucidated. It is recommended to adjust the lowest PEEP sufficient to maintain SpO2 between 90 - 95%, with FiO2 < 60%, PaCO²: between 30-35 mmhg. Hospital Israelita Albert Einstein performs the standard ventilation PCV, VC: 6ml/kg, DRIVING PRESSURE: 15cmH2O, PEEP: 15cmH2O, PaCO²:30-45 mmhg.

In the paragraph above, we can observe few discrepancies related to the initial protocols for admission of MV at COVID-19, ASSOBRAFIR launched in May 2020 a document on physical therapy resources used in intensive care units for the assessment and treatment of respiratory disorders in patients with covid- 19 which recommends MV protocols very similar to the AMIB, diverging only the PaCO2 value and the PEEP titration.

ASSOBRAFIR recommends decremental PEEP titration, aiming at lower driving pressure, even though the literature reports the possibility of adjustments using the PEEP-FIO2 table for low PEEP values, the same used for Respiratory Distress Syndrome (ARDS) , AMIB says that the ideal adjustment for PEEP has not yet been fully elucidated and recommends that this adjustment be made in such a way as to maintain SpO2 values between 90 and 95%. Driving-pressure or driving pressure is a way used in MV to minimize the risk of lung injuries, especially in patients with ARDS. In the Recommendations for intensive support for critically ill patients with suspected or confirmed infection by COVID-19 published by the Hospital Israelita Albert Einstein in 2020, unlike the other institutions mentioned above, it does not offer the volume controlled ventilation (VCV) mode, it only suggests the controlled ventilation mode pressure (PCV), the PEEP titration is defined as 15cmH20, thus we can observe a small difference in the MV protocols of these institutions.

As it is a new disease, some adjustments, conduction and ventilatory parameters may increase the risk of mortality in these patients, as there is no consensus on mechanical ventilation in patients with COVID-19.

II. Methods

The work consisted of a bibliographic review of a documentary and retrospective field through the collection, comparison and correlation of data published in indexed journals in the years 2020 and 2021. This research did not cover any type of therapeutic intervention, only data collection, therefore,it did not offer any kind of direct risk.

Did some assigned parameters or modalities used during mechanical ventilation contribute to the increased risk of mortality in patients with COVID-19?The conduct of mechanical ventilation, regarding ventilatory modalities, adjustments or parameters may be related to the increased mortality of patients who required mechanical ventilation during hospitalization for COVID-19 in the ICU.

III. Results

COVID-19 is a viral infection of the airways that mainly affects epithelial/alveolar and endothelial cells, resulting in desquamation of pneumocytes, presence of hyaline membrane, formation and interstitial inflammation with lymphocyte infiltration. (SHI YU et al. 2020). At the beginning of the pandemic, there were no strategic plans to be applied, as everything was new. Recommendations from the WHO, the Brazilian Ministry of Health, the Centers for Disease Control and Prevention (CDC, USA) and other national and international organizations suggested the application of influenza contingency plans and their tools, due to the clinical and epidemiological similarities between these respiratory viruses. These contingency plans provided for different actions according to the severity of the pandemics.

The diagnosis of COVID-19 is based on the epidemiological history according to clinical criteria, as well as obtaining information about recent travel and residence in areas of communities infected by COVID-19. The start time of COVID-19 is usually between 8-12 days. COVID-19 is a condition associated with many diseases that result in reduced lung compliance and severe hypoxemia. (SHI YU et al. 2020). Approximately 20% of patients with COVID-19 develop severe respiratory problems, with an overall fatality rate around 2.3%. Patients with severe disease usually present with fever, dry cough, dyspnoea, and bilateral pulmonary infiltrates. Occasionally, non-respiratory symptoms, such as palpitation, diarrhea or headache, preceded the respiratory symptoms. Some patients are afebrile onset of disease, the clinical spectrum of COVID-19 ranged from asymptomatic to fatal pneumonia. The rate of infection in asymptomatic patients is not yet defined, as most asymptomatic infections end up with no symptoms. (PARK et al. 2020)

Furthermore, according to Dondorp et al. (2020) several studies were conducted in regions with overburdened health systems, which possibly led to limited resources as a result of higher mortality rates.Due to the high risk of aerosolized airway infection, potentially aerosol-generating procedures such as non-invasive ventilation (NIV) or high-flow nasal cannula (HFNC) therapy are of concern. Avoidance of NIV/HFNC therapy and early tracheal intubation has been suggested as a management strategy for COVID-19; however, this is controversial due to the worse results reported with tracheal intubation (TOBIN, 2020).According to Carvalho et al. (2020) mechanical ventilation replaces and aids spontaneous ventilation and is indicated for cases of both hypercapnic and hypoxemic respiratory failure. It can be non-invasive (NIV) with face masks or invasive (IMV) with the aid of an endotracheal tube or tracheostomy tube. The objective is to improve gas exchange, reduce the work of breathing, increase oxygenation, reduce hypercapnia and metabolic acidosis, in addition to improving the pulmonary ventilation/perfusion (V/Q) ratio.MV cannot correct the physiological response to increased hypoxemia caused by the virus (inflammation, high fever, and increased oxygen demand). Otherwise, it can even worsen these dysfunctions due to lung injury induced by MV. In addition, lung injuries can also be associated with the use of spontaneous MV, thanks to the stress and tension in the lung associated with a high tidal volume added to an increased inspiratory effort, configuring a self-induced lung injury by the patient. cause of lung injury; despite the improvement in survival, its effect on the mortality of these patients is still unknown (GATTINONI et al. 2020).

According to Telias et al. (2020) in situations of sedated patients, atelectasis caused by gravitational forces may occur in dependent lung regions, making the lung region available for gas exchange reduced. The prone position improves oxygenation and ventilates less harmfully, better tolerating NIV. Due to the greater density of pulmonary vessels in the dorsal region, regardless of severity, there is a relative increase in ventilation in this region, resulting in a better V/Q ratio.

Rosenbaum (2020) states that patients who evolve with the most severe forms of the disease may remain hypoxemic for a long period, requiring high parameters of mechanical ventilation and for several sessions of pronation. Although, for these reasons, weaning from mechanical ventilation is being considered with caution, the WHO recommends that weaning protocols be used in which the possibility of spontaneous breathing is assessed daily. With the increase in the disease, an Italian group led an Italian group to describe two phenotypes in COVID-19: L (low) and H (High). According to Ferrando et al. (2020) The H phenotype represents patients with high lung elastance and good response to high PEEP levels, a presentation quite similar to acute respiratory distress syndrome (ARDS).The L phenotype is characterized by low elastance and little or no response to PEEP in alveolar recruitment. Although these are observations without prospective validation, their conclusions allow prioritizing individualized treatment strategies. Alveolar damage is severe, making it essential to implement protective ventilation at risk of inducing further lung injury by the therapy itself if this concept is not implemented (MARINI et al. 2020).

PEEP levels can be quite variable given the heterogeneity of disease presentation, however most of the literature reports levels between 8-12cmH2O (GATTINONI et al. 2020).Guérin et al. (2013) states that recruitment maneuvers can and should be performed. The use of 40 seconds of continuous positive pressure (CPAP) at 40cmH2O is recommended. Recruitment with progressive PEEPs is not recommended. The prone position is effective for improving alveolar recruitment of gravitationally dependent zones16. It is important to stabilize the patient for at least 12 to 24 hours before considering pronation.

The called L lung consists of a light lung, which despite looking like hypoxemia, has a high compliance and makes ventilation "easier". This patient will be able to make a tidal volume between 6-8 ml/kg of predicted weight without large plateau pressures. A PEEP of 10 cmH2O would be sufficient to ensure maintenance of alveolar opening without major associated hypoxemia. Using very high parameters in these patients can induce lung injury and transform an L lung into an H lung, which is much more difficult to ventilate. Type H lung is the classic prototype of ARDS. A very infiltrated lung, heavy and hard on ventilation. It needs high FiO2 and PEEP, with a volume of 6 ml\kg or less, generating high plateau pressures. In these patients, a PEEP of 15 cmH2O seems more adequate and has a better alveolar recruitment effect with improvement in hypoxemia. In this profile, not performing a rigorous protective ventilation strategy (plateau pressure < 30 cmH2O, drive pressure < 15 cmH2O and tidal volume < 6 ml\kg) directly worsens the lung injury, which we call VILI (Ventilator Induced Lung Injury), directly linked to the concepts of biotrauma (volutrauma, atelectrauma and barotrauma) and hinders his exit from ventilation (GATTINONI et al. 2020).

IV. Conclusion

COVID-19 is a disease that is difficult to control in terms of dissemination and treatment, however it was possible to prove in the articles of this study that specific ventilatory care for the pathogenesis found in COVID-19 should have been adopted in order to reduce rates mortality and pulmonary sequelae secondary to the disease. The articles also demonstrate the importance of universal public health and access to means of prevention and control of chronic diseases, such as hypertension and diabetes, which are strongly related to comorbidity factors highly related to death from COVID-19. It was also found that the indiscriminate use of high PEEP, as well as excessive numbers of alveolar recruitment maneuvers may have contributed to the increased mortality of patients with COVID-19, since in cases of the low phenotype, these interventions were not necessary. Finally, care with the driving pressure of patients with a high phenotype was essential to maintain lung integrity. Further studies are still needed in order to promote the prophylactic effects of ventilatory conduction in the face of new infectious diseases and pandemic periods.

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