Comparison between technical parameters recommended by regulatory agencies and relevant institutions for ventilatory therapy equipment used in patients with COVID-19

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Abstract

Background Patients contaminated with the new coronavirus, SARS-CoV-2, and who develop the severe form of the disease require ventilatory support to maintain adequate gas exchange. The objective of this systematic review was to establish reference parameters of ventilator therapy used in the various levels of severity of adult patients affected by COVID-19 to assist health professionals and hospital managers who will purchase this equipment.

Methods It used four databases: Medline, Cochrane Central, Scielo, and Pubmed. Restrictions applied as to the language, restricted to English, and to the patient’s profile, only adults affected by SARS-CoV-2. The review process was carried out by three independent reviewers using the PRISMA-P method.

Results Nineteen articles were included, in addition to the recommendations of the Brazilian Association of Intensive Care Medicine (Brazil), Federal Commission for Protection against Health Risks (Mexico), Medicines and Healthcare Products Regulatory Agency (UK), Pan American Health Organization, and World Health Organization. The types of ventilatory therapies found in the articles eligible for this study were continuous positive airway pressure (CPAP), non-invasive ventilation (NIV), and invasive mechanical ventilation (IMV). For each ventilatory therapy, the parameters presented in the article and the recommendations of regulatory agencies and relevant institutions were compared and analyzed.

Conclusion It was possible to suggest a relationship between the respiratory support strategy adopted by the clinical team and the clinical conditions of the patient infected with SARS-CoV-2. The included studies used ventilation modes and parameters within the specifications and recommendations of relevant regulatory agencies and institutions. However, some minor differences were observed in the instruction presented among the agencies more related to the recommended ventilation modes. Further studies are needed.

Keywords COVID19 · Non-invasive ventilator · Invasive ventilator · Mechanical ventilator support · Artificial respiratory

Introduction

A new coronavirus (SARS-CoV-2) was identified in Wuhan province, China, in December 2019, and on March 11, 2020, the World Health Organization declared a state of a pandemic for coronavirus 2019 (COVID-19) (Cucinotta and Vanelli 2020; Ducharme 2020). Virus transmission occurs mainly by contact and respiratory droplets (World Health Organization (WHO) 2020a). Based on epidemiological evidence (World Health Organization (WHO) 2020b), it was identified that its incubation period could vary between one and 14 days, being more frequent from five to six days (Lima 2020). The main clinical manifestations observed are fever, fatigue, and dry cough (Lima 2020; World Health Organization (WHO) 2020b). However, in critical conditions
of the disease, patients may present with acute respiratory distress syndrome (ARDS), sepsis, metabolic acidosis, and rapidly evolving coagulation dysfunction (Huang et al. 2020; Wang et al. 2020a; Chen et al. 2020).

ARDS is a life-threatening form of lung injury. This lung injury may result from a primary lesion to the lung parenchyma, such as pneumonia or aspiration, or from a systemic process, such as sepsis or trauma. The increase in capillary permeability, leading to inflammation, is the inciting factor for ARDS. Damage to the capillary endothelium and alveolar epithelium results in the accumulation of proteins in the alveoli, activation of pro-inflammatory cytokines, and pulmonary fibrosis. This cascade of events leads to the loss of functional lung tissue and the chest radiography shows bilateral opacities. As ARDS progresses, lung compliance decreases with hypoxemia, and patients may progress to ventilator dependence (Fan et al. 2018; Pierrakos 2012).

The Berlin definition published in 2012 established diagnostic criteria for ARDS (Ranieri et al. 2012). In it, ARDS was classified into three categories according to the severity and mortality found in previous multicenter studies. Thus, to stratify the severity of the lung injury, the PaO2/FiO2 ratio (which is the ratio between the arterial partial pressure of oxygen (PaO2) and the fraction of inhaled oxygen (FiO2)) was associated with the positive end-expiratory pressure (PEEP) (Ranieri et al. 2012).

These patients are categorized concerning to PaO2/FiO2. They are classified as having severe ARDS when this ratio is less than or equal to 100 mmHg; when this ratio is between 101 and 200 mmHg, they are classified as moderate ARDS; and, when it is between 201 and 300 mmHg, they are classified as mild ARDS. All frames associated with a PEEP equal to or greater than 5 cmH2O (Ranieri et al. 2012). Therefore, the Berlin definition intended to assist in the diagnosis and prognosis of the patient. This classification corroborates in the decision of the mechanical ventilation protocol used, such as specific parameter adjustments, the need for alveolar recruitment, and the decision to use the prone position (Simões 2018).

Around 5% of patients infected with the new coronavirus develop the severe form of the disease requiring ventilatory support as a strategy to assist adequate gas exchange (World Health Organization (WHO) 2020b). And so, the technique proposed by Brower et al. (2000) for patients with ARDS can be applied. Protective mechanical ventilation is indicated for the management of ARDS, and consists of the use of tidal volumes equal to or less than 6 ml/kg of predicted body weight (PBW) and plateau pressure limited to 30 cmH2O, to avoid barotrauma and volutrauma (Brower et al. 2000). And for that, it should have equipment that meets the needs of ventilatory adjustments according to the clinical severity of the patient, to provide, in an appropriate way, the time necessary for the organism to have the best recovery conditions.

It was observed that patients with a severe clinical picture of COVID-19, despite having ARDS criteria, present good pulmonary compliance, but severe hypoxemia (Guimarães 2020). This was due to disturbances in the perfusion, caused by the development of micro thrombosis. As there was no blood circulating in the alveolus properly, despite lung ventilation (Marini and Gattinoni 2020). Due to this peculiarity, it was noticed that there was no difference between the adoption of high or low PEEP, and thus, an intermediate PEEP less than or equal to 15 cmH2O was established as a treatment strategy in severe cases (Marini and Gattinoni 2020).

Given the specificity regarding the adequate adjustments of the ventilatory parameters to be used, as well as the coincidence resulting from the lack of pulmonary ventilators in intensive care units (ICUs), during the peak of the pandemic in several countries, different alternatives appeared to minimize the respiratory distress of the patients. But it did not take into account the minimum parameters that ventilatory therapy equipment should have to attend to patients with COVID-19. Based on this, several international organizations decided to disclose the minimum characteristics of the equipment to be used in respiratory therapy units as a way to streamline their production and distribution (Associação de Medicina Intensiva Brasileira 2020; Comisión Federal para la Protección contra Riesgos Sanitarios 2020; Medicines and Healthcare Products Regulatory Agency 2020; Pan American Health Organization (PAHO) 2020; World Health Organization (WHO) 2020a, c). Other alternatives have also been suggested, such as the use of anesthesia equipment like a mechanical ventilator, the use of a transport ventilator, and the sharing of the same equipment with more than one patient, for example (Notz et al. 2020).

The objective of this systematic review was to establish reference parameters of ventilatory therapy used in the various levels of severity of adult patients affected by COVID-19, to assist health professionals and hospital managers who will purchase this equipment. The hypothesis of this study was that ventilatory parameters can be established according to the patient’s clinical conditions. Besides that, the study made a comparison with the minimum specifications of artificial ventilation equipment proposed by regulatory agencies and relevant institutions to identify gaps, divergences, and correlations in these guidelines.

**Methods**

This systematic review used the methodology followed as presented by Moher et al. (2015) called Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA-P).
**Study design**

The protocol defined by the PRISMA-T guidelines was followed. Thus, the entire review process of the articles was carried out by three reviewers and their summary is in the PRISMA flow diagram shown in Fig. 1.

**Inclusion/exclusion criteria**

To carry out this study, the language restriction that was applied was limited to English, which is a universal language. As for the patient’s profile, articles referring to the care of children and newborns were excluded. Therefore, it focuses on adult patients affected by SARS-CoV-2. We considered epidemiological studies, cross-sectional studies, case studies, clinical observations, and reports from randomized health agencies related to respiratory diseases associated with COVID-19. The research was limited to articles published between January 1, 2020, and May 8, 2020. A bibliographic review was conducted between April and May 2020.

**Search sources**

For this study, four databases indicated for COVID-19 were used: Cochrane Central, MEDLINE, PUBMED, and SCIELO. The following keywords were used to carry out this systematic review: “COVID19,” “COVID-19,” “coronavirus,” “ventilator,” “respirator,” “non-invasive ventilator,” “non-invasive mechanical ventilator,” “invasive ventilator,” “mechanical ventilator,” “mechanical ventilator support,” “ventilatory,” “respiratory,” and “artificial.” Two authors analyzed the articles for titles and full abstracts.

**Ventilation parameters included interventions and outcomes**

There were no restrictions.

**Selection**

Two authors independently analyzed the titles and abstracts of all studies identified in the research strategy and discarded those that were duplicated. The studies considered eligible were reassessed by reading their full texts, which make up this systematic review. In cases where a disagreement occurred on the chosen articles, the opinion of the third author was requested. The selection process for this study is shown in Fig. 1.

**Data collection**

Two authors extracted data from the selected articles, as well as their accuracy and fidelity, and a third author resolved the disagreements that arose throughout the process.

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**Fig. 1 Flow chart—PRISMA**
**Assessment of bias quality and risk of included studies**

As this study is an assessment referring to SARS-CoV-2, mainly, with preliminary results, no methodological quality assessment was carried out. However, the search for articles was carried out only in reliable databases and with quality already recognized.

**Results**

After searching the referenced databases and using the keywords presented, 922 references were found that had in their titles, abstracts, or keywords the terms used in the search. Following, duplicate files were identified and 206 were removed.

In the next stage, the justified exclusion of the articles was carried out, according to previously defined inclusion and exclusion criteria, excluding 49 other articles. When reading the titles and abstracts, 648 articles were excluded by the inclusion/exclusion criteria presented in the methods. Thus, for the development of this work, 19 articles were eligible, as shown in Fig. 1.

Within the selected articles, references were found to the following types of ventilatory therapies: continuous positive airway pressure (CPAP), non-invasive ventilation (NIV), and invasive mechanical ventilation (IMV). Table 1 shows the list of the ventilatory types found with the respective references.

The nineteen articles selected for this work are listed in Table 2, including the name of the first author, the article title, and the respective approach found in each one.

In the articles of Bai et al. (2020), KeAi (2020a, b), Peng et al. (2020), and Vitacca et al. (2020), they proposed a classification of patient’s clinical status and divided them into four categories: mild or green; moderate or common, or yellow; severe or orange; and, critical or red.

Table 3 shows the symptoms presented by the patients in each category and the indication of the treatment strategy. Thus, it was possible to understand the clinical need applied to combat the symptoms of coronavirus and, thus, understand the ventilatory parameters used in practice for this.

As can be seen, patients with mild cases tend to have an O$_2$ saturation greater than 94%, with a respiratory rate less than or equal to 20 bpm and may be asymptomatic. In a moderate state, O$_2$ saturation may be less than 94% with a respiratory rate greater than 20 bpm, and pneumonia may occur. In this case, the WHO (Peng et al. (2020) does not recommend the use of oxygen therapy, but other authors already recommend the use of this type of therapy (Bai et al. (2020); KeAi (2020a; Peng et al. (2020)) even with the flow definition in the range of 10–15 L/min (Vitacca et al. (2020)).

In severe and critical cases, support ventilation is recommended. Severe cases, for example, presented in the studies with PaO$_2$/FiO$_2$ ≤ 300 mmHg, SpO$_2$ ≤ 93%, and RR ≥ 30 bpm, indicating the use of CPAP and NIV with constant monitoring (Bai et al. (2020); KeAi (2020a, b; Peng et al. (2020). However, in such cases, if the patient gets worse, switch immediately to invasive ventilation. Critical cases had indications of CPAP, NIV, and IMV with protective mechanical ventilation: tidal volume of 4–8 ml/kg of predicted body weight and plateau pressure < 30 mmH2O. All of these data are shown in Table 3.

After understanding the relationship between the classification of the patient’s clinical status with the ventilatory parameters, we sought to relate the characteristics of these parameters used in respiratory therapy with the different types of ventilation, limited to those found in the articles eligible for this study. The results are presented in Table 4 through a specific relationship between the equipment’s adjustment parameters and the type of ventilatory support used (CPAP, NIV, and IMV).

Thus, in the case of using CPAP, the parameters for use in critical and severe cases are presented according to their characteristics. For the use of NIV, the characteristics of this type of ventilatory support and the parameters that meet them were also presented. As can be seen in Table 4, the parameters of CPAP and NIV overlap, and it is up to the clinical team to define the best respiratory therapy technique to be applied to the patient.

In cases of IMV, there are a lot more citations and parameter settings. In this sense, the parameters of tidal volume, plateau pressure, FiO$_2$, respiratory rate, PEEP, among others were presented as referenced by the authors of the articles in

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**Table 1** Relationship between ventilation types and related articles

| Type of ventilation | Related articles |
|---------------------|-----------------|
| Continuous positive airway pressure (CPAP) | (Lazzeri et al. 2020; Radovanovic et al. 2020) |
| Non-invasive ventilation (NIV) | (Bai et al. 2020; Dondorp et al. 2020; KeAi 2020a, 2020b; Lazzeri et al. 2020; Meng et al. 2020; Möhlenkamp and Thiele 2020; Peng et al. 2020; Vitacca et al. 2020; Zhang et al. 2020) |
| Invasive mechanical ventilation (IMV) | (Bai et al. 2020; Dondorp et al. 2020; Gage et al. 2020; KeAi 2020a, b; Kluge et al. 2020; Lazzeri et al. 2020; Mauri et al. 2020; Möhlenkamp and Thiele 2020; Pedersen et al. 2020; Peng et al. 2020; Wang et al. 2020b; Zhang et al. 2020) |
Table 2  Presentation of the articles found with the name of the first author, the article title, and approach presented

| Author | Title of the article | Approach |
|--------|----------------------|----------|
| Alhazzani et al. 2020 | Surviving Sepsis Campaign: Guidelines on the Management of Critically Ill Adults with Coronavirus Disease 2019 (COVID-19) | The article presents recommendations classified as best practices, strong, weak, and not recommended for managing adult patients with COVID-19. |
| Bai et al. 2020 | Chinese experts’ consensus on the Internet of Things-aided diagnosis and treatment of coronavirus disease 2019 (COVID-19) | It presents the nCapp system, used to monitor the evolution of the disease. Cases confirmed by the system are classified by doctors as mild, moderate, severe, and critical. Presents case management strategies, including the use of invasive mechanical ventilation (IMV). |
| Dondorp et al. 2020 | Respiratory Support in Novel Coronavirus Disease (COVID-19) Patients, with a Focus on Resource-Limited Settings | The authors present current guidelines on the best provision of ventilatory support, considering environments with limited resources, for the management of patients with COVID-19. |
| Gage et al. 2020 | Reacquainting Cardiology With Mechanical Ventilation in Response to the COVID-19 Pandemic | A brief review of the acute respiratory discomfort syndrome (ARDS) is presented and presents a general review of invasive mechanical ventilation (IMV), breathing modes, and parameters for pulmonary protection ventilation. |
| Guimarães 2020 | Approach of the physiotherapist in intensive care units in the context of the COVID-19 pandemic | The author discusses the role of physiotherapists in the treatment of patients with COVID-19 and presents recommendations on the use of protective ventilation, and the individual adjustment of PEEP in the pulmonary ventilator. Addresses the adoption of a prone position. |
| KeAi 2020a | Diagnosis and treatment plan of Corona Virus Disease 2019 (tentative sixth edition) | It is a guideline in its fifth revision, the Corona Virus Disease Diagnosis and Treatment Plan 2019. It presents the characteristics of coronavirus pathogens, clinical characteristics, case definitions, differential diagnosis, identification and reporting of cases, treatment, transfer principles, and hospital infection control. |
| KeAi 2020b | Interpretation of the diagnosis and treatment plan of Corona Virus Disease 2019 (tentative fifth revised edition) | Features updates between previous versions and the current version of the Guideline Corona Virus Disease Diagnosis and Treatment Plan 2019 (Diagnosis and treatment plan of Corona Virus Disease 2019). |
| Kluge et al. 2020 | German recommendations for critically ill patients with COVID-19 | The authors present recommendations for the management of patients with COVID-19, in any severity of the disease, from symptoms, clinical analyzes, exams, results, and ventilatory support. |
| Lazzeri et al. 2020 | Respiratory physiotherapy in patients with COVID-19 infection in acute setting: a Position Paper of the Italian Association of Respiratory Physiotherapists (ARIR) | The document prepared by the Italian Association of Respiratory Physiotherapists in support of the Italian Association of Physiotherapy and presents the practices adopted in coping with patients with COVID-19. Addresses non-invasive and invasive ventilatory support practices. |
| Mauri et al. 2020 | Potential for Lung Recruitment and Ventilation-Perfusion Mismatch in Patients With the Acute Respiratory Distress Syndrome From Coronavirus Disease 2019 | The authors present specific pathophysiological characteristics of the coronavirus 2019 acute respiratory distress syndrome. The report studies using low and high PEEP in a group of patients and comparing the results obtained using electrical impedance tomography (EIT). |
| Meng et al. 2020 | Intubation and Ventilation amid the COVID-19 Outbreak: Wuhan’s Experience | The authors report the experience of treating critically ill patients with COVID-19 in Wuhan. It addresses, among other points, about timely and not premature intubation, as a crucial strategy to combat a progressive oxygen debt and about the protective ventilation of the lungs. Presents intubation strategies widely used in Wuhan. |
| Möhlenkamp and Thiele 2020 | Ventilation of COVID-19 patients in intensive care units | This review presents how the ventilation of patients with COVID-19 in the intensive care unit (ICU) is challenging because of the heterogeneity of lung pathology. Addresses the importance of individualized lung protection as a ventilation strategy to improve the outcome. |
| Pedersen et al. 2020 | Initial experiences from patients with COVID-19 on ventilatory support in Denmark. | It presents an evaluation of 16 patients with COVID-19 admitted to the intensive care unit (ICU) of a hospital due to respiratory failure. The authors present clinical parameters of the patients and, among others, the ventilatory support strategies used. |
the treatment of patients with COVID-19. The study and knowledge of the limits of these parameters applied in clinical practice, as found in the eligible articles, will be important for the analysis of this work. For a more complete view of the parameters, see Table 4.

At this point, based on the clinical characteristics of patients who are treated with COVID-19, as well as knowledge of ventilatory parameters and types of respiratory therapy, Table 5 shows the basic characteristics of mechanical ventilation equipment that can be used based on the specifications of international regulatory agencies and relevant institutions such as AMIB (Brazil), CFPRS (Mexico), MHRA (UK), and the World Health Organization (WHO/PAHO) (Associação de Medicina Intensiva Brasileira 2020; Comisión Federal para la Protección contra Riesgos Sanitarios 2020; Medicines and Healthcare Products Regulatory Agency 2020; Pan American Health Organization (PAHO) 2020; World Health Organization (WHO) 2020a, c).

All the characteristics defined by these organs were found to be fundamental for the production of respiratory support equipment necessary for use in patients with COVID-19 or even acquisition. In these characteristics, data related to tidal volume, respiratory rate, PEEP, and modes of operation can be found. In the last column of Table 5, the parameters actually found in the practical use of the treatment of COVID-19 are presented, at its most extreme limits. This is to demonstrate that some of the characteristics defined by international organizations, within the proposed minimum specifications, may not efficiently meet the routine care of patients infected by SARS-CoV-2. The importance of this relationship lies in the comparison between clinical practice parameters and the technical specifications proposed by different institutions. These configurations may define a basic model of respiratory support equipment to be used in patients with COVID-19.

Another result found in this work is related to the lack of some information on basic characteristics that should be mentioned in the articles eligible and related to the equipment used. Despite the concern of regulatory agencies and relevant institutions to present the minimum ventilation modes, monitoring modes, and alarms, these are not mentioned in the articles. Table 6 lists characteristics recommended by regulatory agencies and relevant institutions and not mentioned in the articles eligible for this systematic review.

**Discussion**

This systematic review of articles on ventilatory assistance in patients with COVID-19 demonstrated that it was possible to establish a relationship between the clinical condition of the patient infected with SARS-CoV-2 and the type of ventilation support to be adopted. Patients with severe conditions were preferably treated with CPAP and NIV and patients with critical conditions and severe hypoxemia were treated with IMV, as shown in Table 3. The most used ventilatory modes for IMV and found in 14 of the eligible articles were pressure-assisted/controlled ventilation, volume assisted/controlled ventilation, synchronized intermittent mandatory ventilation.
| Classification          | Authors | Related clinical parameters                                                                 | Recommended treatment                                                                 |
|------------------------|---------|---------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------|
| Mild or green          | KeAi 2020a, b; Peng et al. 2020 | - Mild and nonspecific clinical symptoms  
                        - Mild fever, mild fatigue, mild cough, anorexia, malaise, myalgia, sore throat, dyspnea, nasal congestion, and/or headache;  
                        - Usually with asymptomatic infection;  
                        - Rarely have diarrhea, nausea, and vomiting;  
                        - No signs of pneumonia (assessed by image—computed tomography); | Monitoring, general treatment, symptomatic treatment, antiviral treatment. |
|                        | Bai et al. 2020; KeAi 2020a, 2020b; Peng et al. 2020 | - Specific clinical symptoms  
                        - Fever and problems with the respiratory tract; | General treatment, symptomatic treatment, antiviral treatment. Comments: |
|                        | Vitacca et al. 2020 | - Pneumonia can be seen on the image by computed tomography; | (Peng et al. 2020) WHO does not recommend oxygen therapy for patients with this condition; |
|                        | | | (Bai et al. 2020; KeAi 2020a, 2020b; Peng et al. 2020) Oxygen therapy is recommended; |
|                        | | | (Vitacca et al. 2020) Respond with oxygen therapy of 10–15 L/min. |
| Moderate or common, or yellow | KeAi 2020b; 2020a | - Specific clinical symptoms  
                        - Fever and problems with the respiratory tract; | General treatment, symptomatic treatment, antiviral treatment, and respiratory therapy indicated: |
|                        | Bai et al. 2020; KeAi 2020a, 2020b; Peng et al. 2020 | - Pneumonia can be seen on the computed tomography and one of the following symptoms:  
                        - Patients with lesion progression >50% within 24 to 48 h on pulmonary imaging should be treated as severe cases;  
                        - PaO₂/FiO₂ ≤ 300 mmHg;  
                        - SpO₂≤93%;  
                        - RR≥30 bpm; | CPAP;  
                        - NIV, oxygen fraction (FiO₂) <50%;  
                        - NIV with constant Monitoring and up to a maximum of 2 h, if the discomfort does not improve or there is a worsening of the condition, switch to invasive ventilation immediately. |
|                        | Vitacca et al. 2020 | - SpO₂<94%;  
                        - RR>20 bpm. | General treatment, symptomatic treatment, antiviral treatment, and respiratory therapy indicated:  
                        - CPAP;  
                        - NIV with constant monitoring and up to a maximum of 2 h, if the discomfort does not improve or there is a worsening of the condition, move to invasive ventilation immediately;  
                        - IMV with protective mechanical ventilation: tidal volume of 4–8 ml/kg of predicted body weight and plateau pressure<30 mmH₂O. |
| Severe or orange        | KeAi 2020b | - Dyspnea and/or hypoxemia, usually within a week of the onset of the disease, may progress rapidly, septic shock, difficult to balance metabolic acidosis, bleeding and coagu lation dysfunction or respiratory distress; | General treatment, symptomatic treatment, antiviral treatment, and respiratory therapy indicated:  
                        - CPAP;  
                        - NIV with constant monitoring and up to a maximum of 2 h, if the discomfort does not improve or there is a worsening of the condition, move to invasive ventilation immediately;  
                        - IMV with protective mechanical ventilation: tidal volume of 4–8 ml/kg of predicted body weight and plateau pressure<30 mmH₂O. |
|                        | Bai et al. 2020; KeAi 2020a | - Pneumonia seen by computed tomography and showing one of the following symptoms:  
                        - Patients with lesion progression >50% within 24 to 48 h on pulmonary imaging should be treated as severe cases;  
                        - PaO₂/FiO₂<100 mmHg;  
                        - SpO₂<94%;  
                        - RR>30 bpm and poor response to oxygen therapy 10–15 L/min;  
                        - CPAPe/VNI with FiO₂>50% or PaO₂/FiO₂<200 mmHg  
                        | | |
|                        | Peng et al. 2020 | - SpO₂<94% and 25≤RR≤30 bpm and poor response to oxygen therapy 10–15 L/min;  
                        - CPAPe/VNI with FiO₂>50% or PaO₂/FiO₂<200 mmHg  
                        | | |

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\(SpO_2\), peripheral oxygen saturation  
\(RR\), respiratory rate  
\(PaO_2/FiO_2\), the ratio of (arterial oxygen pressure) divided by the (inspired oxygen fraction)  
\(ICU\), intensive care unit  
\(CPAP\), continuous positive airway pressure  
\(NIV\), non-invasive ventilation  
\(IMV\), invasive mechanical ventilation  
\(bpm\), breath per minute
### Table 4  Ventilation type with parameters used by the author

| Ventilation type                              | Authors                                      | Ventilatory parameters                                                                                                                                 |
|-----------------------------------------------|----------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------|
| Invasive mechanical ventilation (IMV)         | (Bai et al. 2020; KeAi 2020a, 2020b; Wang et al. 2020b) | Parameters:  
  - Tidal volume: 4–8 ml/kg of PBW;  
  - Plateau pressure < 30 cmH₂O.  
  Note: Wang et al. (2020b) recommend ventilation prone to patients with a PaO₂/FiO₂ < 150 mmHg for more than 12 h. |
|                                               | (Kluge et al. 2020)                          | Ventilation mode:  
  - Synchronized intermittent mandatory ventilation (SIMV) or pressure-controlled ventilation (PCV).  
  Parameters:  
  - FiO₂ 90–95%;  
  - Tidal volume: 6–8 ml/kg of PBW;  
  - Plateau pressure ≤ 30 cmH₂O.  
  Note: Kluge et al. (2020) recommend ventilation prone to patients with a PaO₂/FiO₂ < 150 mmHg for more than 16 h. Patients unable to meet these parameters were ventilated in the prone position. |
|                                               | (Meng et al. 2020)                           | Parameters:  
  - RR > 30 bpm;  
  - PaO₂/FiO₂ < 150 mmHg. |
|                                               | (Mauri et al. 2020)                          | Parameters:  
  - PEEP: 5–15 cmH₂O. |
|                                               | (Dondorp et al. 2020)                        | Ventilation mode:  
  - Controlled ventilation (CV).  
  Parameters:  
  - Tidal volume ≤ 6 mL/kg of PBW;  
  - RR ≤ 35 bpm;  
  - Blood pH > 7.2;  
  - SpO₂ > 88%.  
  Ventilation mode:  
  - Pressure support ventilation (PSV).  
  Parameters:  
  - Tidal volume > 6 ml/kg of PBW;  
  - PEEP ≤ 12 cmH₂O.  
  Note: Dondorp et al. (2020) recommend ventilation prone for at least 16 h; patients can be ventilated at a low conduction pressure, less than 15 cmH₂O, usually as low as 5–7 cmH₂O. |
|                                               | (Pedersen et al. 2020)                       | Parameters:  
  - Tidal volume ≤ 6 ml/kg of PBW;  
  - Plateau pressure ≤ 30 cmH₂O.  
  Parameters for COVID-19 initial phase:  
  - PEEP ≤ 18 cmH₂O;  
  - FiO₂ 0.7–0.8 with an average of 0.62, maximum 1.00. |
|                                               | (Guimarães 2020)                             | Parameter:  
  - PaO₂/FiO₂ < 150, in prone position. |
|                                               | (Lazzeri et al. 2020)                        | Parameters: Prone position (12–16 h/day):  
  - PaO₂/FiO₂ ≥ 150 mmHg;  
  - PEEP ≤ 10 cmH₂O;  
  - FiO₂ ≤ 0.60. |
|                                               | (KeAi 2020a; Peng et al. 2020; Vitacca et al. 2020) | Parameters: Critical cases:  
  - SpO₂ < 94%;  
  - RR > 30 bpm, no response to oxygen 10–15 L/min. |
|                                               | (Zhang et al. 2020)                          | Parameters:  
  - Tidal volume: 4–8 ml/kg of PBW;  
  - Plateau pressure < 30 cmH₂O.  
  Indication when parameters are:  
  - SpO₂ < 93%;  
  - RR > 35 bpm;  
  - Tidal volume: 9 ml/kg of PBW. |
|                                               | (Möhlenkamp and Thiele 2020)                 | Parameters: |
(SIMV), and pressure support ventilation. Fifteen out of the nineteen selected articles used ventilatory parameters within the recommended limits of protective mechanical ventilation, that is, a tidal volume between 4 and 6 ml/kg of PBW and a plateau pressure limited to 30 cmH₂O.

The CPAP and NIV techniques are generally used at the beginning of the respiratory syndrome process, and the patient undergoing any of these techniques is under observation for a period. It can be seen in Table 3 that the application of CPAP and NIV techniques occurred according to the Berlin definition at a level of PaO₂/FiO₂ ≤ 300 mmHg. These patients should be kept under observation for at least an hour, and if there was no improvement in physiological parameters or worsening of the condition, the team should place the patient on invasive mechanical ventilation (Lazzeri et al. 2020).

It was noticed that NIV was used to indicate cases of respiratory distress, of mild hypoxemia, with precautions in the release of aerosols to avoid viral transmission to the team (Bai et al. 2020; KeAi 2020a; Peng et al. 2020; Vitacca et al. 2020).

As presented by Gage et al. (2020), controlled assisted ventilation was among the most used modes of ventilation in intensive care units. In controlled assisted ventilation, it is possible to control the pressure or volume administered by the ventilator regardless of whether the respiratory cycle is triggered by the ventilator or by the patient. In controlled pressure ventilation, a defined pressure is delivered to the patient in each breath, while in volume-controlled ventilation, a previously adjusted tidal volume occurs. The parameters of FiO₂, PEEP, and respiratory rate (RR) are also adjusted in these modes.

Gage et al. (2020) further demonstrated that PEEP and FiO₂ can directly affect oxygenation, while the clearance of carbon dioxide was maintained by minute ventilation (product between respiratory rate and tidal volume). Marini and Gattinoni (2020) identified that the use of high PEEP and alveolar recruitment maneuvers was controversial for patients with COVID-19, as there were those who presented severe hypoxemia without changes in lung compliance. These individuals did not respond well to the increase in PEEP. Therefore, PEEP should be adjusted individually.

Table 5 shows that the ventilatory modes found in the articles of this work are as follows: SIMV (Kluge et al. 2020), PCV (Kluge et al. 2020), controlled ventilation (CV) (Dondorp et al. 2020), and pressure support ventilation (PSV) (Dondorp et al. 2020). As can be seen, both the Brazilian Association of Intensive Care Medicine (Brazil) and the Medicines Healthcare products Regulatory Agency (UK) did not include pressure support as a ventilation
| Parameters | AMIB (Brazil) | MHRA (UK) | CFPRS (Mexico) | WHO Interim Guidance | WHO Interim Guidance | WHO Interim Guidance | WHO Interim Guidance | PAHO/WHO | PAHO/WHO | Features |
|------------|--------------|-----------|----------------|---------------------|---------------------|---------------------|---------------------|---------|---------|----------|
|             | Mechanical ventilator | Rapidly manufactured ventilator system (RMVS) | Mechanical ventilator | Invasive ventilator | Ventilator for transport | Continuous positive airway pressure (CPAP) | Bilevel positive airway pressure (BIPAP) | Portable ventilator |
| Tidal volume (ml) | 50–700 | 400±10 (350–450) | 2–2000+ (general use) | 20–2000 | 20–1000 | Unplanned | Unplanned | Unplanned | 1000 | Up to 9 ml/kg of PBW<sup>a</sup> (Zhang et al. 2020)* |
| Respiratory rate (bpm) | 8–40 | 10–30 (increments +2 only mandatory mode) | 0–150 | 0–20 (minimum) | Unplanned | 3–20 | 4–25 | 4–25 | Unplanned | Up to 20 PEEP ≤18 cmH<sub>2</sub>O (Pedersen et al. 2020) |
| PEEP<sup>b</sup> (cmH<sub>2</sub>O) | 0–20 | 5–20 increments +5 | 0–20 | 0–20 (minimum) | Unplanned | 3–20 | 4–25 | 4–25 | Unplanned | Synchronized intermittent mandatory ventilation (SIMV); (PCV) (Kluge et al. 2020); Controlled ventilation (CV); pressure support ventilation (PSV); (Dondorp et al. 2020) |
| Assist/control (A/C) mode | Yes (PCV<sup>c</sup> and/or VCV<sup>d</sup>) | Yes | Yes, assisted pressure (A/C-PCV) | Yes (PCV, VCV) | Unplanned | Unplanned | Yes (PCV) | Yes (PCV and VCV) Unplanned Unplanned Yes (PCV) | Synchronized intermittent mandatory ventilation (SIMV); (PCV) (Kluge et al. 2020); Controlled ventilation (CV); pressure support ventilation (PSV); (Dondorp et al. 2020) |
| A/C volume breaths | Unplanned | Yes | Yes | Unplanned | Unplanned | Unplanned | Unplanned | Unplanned | Unplanned | SIMV<sup>e</sup> mode | SIMV volume breaths | SIMV pressure breaths | SIMV pressure support breaths | Spontaneous/CPAP mode | Non-invasive ventilation |
| SIMV<sup>e</sup> mode | Unplanned | Unplanned | Yes | Yes | Unplanned | Unplanned | Unplanned | Unplanned | Unplanned | Unplanned | Unplanned | Unplanned | Unplanned | Unplanned | Unplanned | | | |
| SIMV volume breaths | Unplanned | Unplanned | Yes | Yes | Unplanned | Unplanned | Unplanned | Unplanned | Unplanned | Unplanned | Unplanned | Unplanned | Unplanned | Unplanned | Unplanned | | | |
| SIMV pressure breaths | Unplanned | Unplanned | Yes | Yes | Unplanned | Unplanned | Unplanned | Unplanned | Unplanned | Unplanned | Unplanned | Unplanned | Unplanned | Unplanned | Unplanned | | | |
| SIMV pressure support breaths | Unplanned | Unplanned | Yes | Yes | Unplanned | Unplanned | Unplanned | Unplanned | Unplanned | Unplanned | Unplanned | Unplanned | Unplanned | Unplanned | Unplanned | | | |
| Spontaneous/CPAP mode | Unplanned | Unplanned | Yes | Yes | Unplanned | Unplanned | Unplanned | Unplanned | Unplanned | Unplanned | Unplanned | Unplanned | Unplanned | Unplanned | Unplanned | | | |
| Non-invasive ventilation | Unplanned | Unplanned | Yes | Yes | Unplanned | Unplanned | Unplanned | Unplanned | Unplanned | Unplanned | Unplanned | Unplanned | Unplanned | Unplanned | Unplanned | | | |

<sup>a</sup> PBW, predictable body weight
<sup>b</sup> PEEP, positive end-expiratory pressure
<sup>c</sup> PCV, pressure-controlled ventilation
<sup>d</sup> VCV, volume-controlled ventilation
<sup>e</sup> SIMV, synchronized intermittent mandatory ventilation

* Neri’s (2020) definition of tidal volume calculation for males: [50 + 0.91 × (height in cm − 152.4)] and for females: [45.5 + 0.91 × (height in cm − 152.4)] or definition of Dondorp et al. (2020) for males: [height (in cm) − 105] and females: [height (in cm) − 110]. Tidal volume calculated according to Dondorp et al. (2020) for male patient, height of 1.90 m, considering 9 ml/kg, equal to 765 ml
modality; however, this mode of ventilation is commonly used at the time of the patient’s weaning (Associação de Medicina Intensiva Brasileira 2020; Medicines and Healthcare Products Regulatory Agency 2020).

The SIMV ventilation mode was also not found in the specifications presented by the Brazilian Association of Intensive Care Medicine (Brazil) nor by the Medicines Healthcare products Regulatory Agency (UK), being considered in the minimum specifications of the Federal Commission for Protection against Health Risks (Mexico) and WHO (World Health Organization (WHO) 2020c). Still, about ventilatory modes, all agencies presented recommendations on controlled ventilation; however, only the MHRA-UK and the Federal Commission for Protection against Health Risks (Mexico) considered the need to include assisted ventilation (Associação de Medicina Intensiva Brasileira 2020; Comisión Federal para la Protección contra Riesgos Sanitarios 2020; Medicines and Healthcare Products Regulatory Agency 2020).

Regarding the tidal volume parameter, most articles found an operating range between 4 and 8 ml/kg of PBW. However, the article of Zhang et al. (2020) had an indication of use up to 9 ml/kg of PBW. Thus, AMIB (Brazil) and MHRA (UK) would not meet the demand for this protocol for patient care. Although, in the case of MHRA (UK), this protocol could be met with the inclusion of the tidal volume with an optional range, 250–800 ml (Associação de Medicina Intensiva Brasileira 2020; Medicines and Healthcare Products Regulatory Agency 2020). As noted, the parameter was met with the ventilator configurations provided by Federal Commission for Protection against Health Risks (Mexico) (Comisión Federal para la Protección contra Riesgos Sanitarios 2020) and WHO (World Health Organization (WHO) 2020c), as they vary within the 20–2000 ml range of tidal volume.

The respiratory rate with the standard specification presented by MHRA (UK) (Medicines and Healthcare Products Regulatory Agency 2020) was in the limited range between

### Table 6 Characteristics presented by regulatory agencies and relevant institutions and not mentioned in the articles eligible for this work

| Parameters/ventilation mode/monitoring/alarms | References |
|---------------------------------------------|------------|
| Parameter: IE ratio; Alarm: Loss of PEEP.  | (Comisión Federal para la Protección contra Riesgos Sanitarios 2020; Medicines and Healthcare Products Regulatory Agency 2020; Pan American Health Organization (PAHO) 2020) |
| Parameter: Inspiratory flow rate (Lpm); Alarm: High pressure; gas supply failure. | (Associação de Medicina Intensiva Brasileira 2020; Comisión Federal para la Protección contra Riesgos Sanitarios 2020; Pan American Health Organization (PAHO) 2020; World Health Organization (WHO) 2020c) |
| Parameter: Inspiratory pressure (cmH2O); Alarm: Power failure. | (Comisión Federal para la Protección contra Riesgos Sanitarios 2020; Medicines and Healthcare Products Regulatory Agency 2020; Pan American Health Organization (PAHO) 2020; World Health Organization (WHO) 2020c) |
| Parameter: Pressure support (cmH2O); Alarm: Low minute volume; high minute volume; vent inoperative; self-diagnostics. | (Pan American Health Organization (PAHO) 2020) |
| Parameter: Leak compensation; Ventilation mode: Spontaneous with timed backup; Alarm: High PEEP; occlusion. | (Comisión Federal para la Protección contra Riesgos Sanitarios 2020) |
| Ventilation mode: Ventilation regulated by pressure and guaranteed in manual or automatic volume assisted/controlled and SIMV, Con guaranteed the volume limit for CPAP ventilation. Spontaneous the pressure of support the ASV the auto the volume control plus, and the volume support (VS) the ventilation with spontaneous and controlled minute volume. | (World Health Organization (WHO) 2020c) |
| Ventilation mode: Peak inspiratory pressure; mean airway pressure; spontaneous minute volume; inspiratory time; expiratory time; Alarm: High/low flow; high/low temperature. | (Comisión Federal para la Protección contra Riesgos Sanitarios 2020; Pan American Health Organization (PAHO) 2020; World Health Organization (WHO) 2020c) |
| Alarm: Low/high FiO2; apnea; breathing circuit disconnect; low battery. | (Medicines and Healthcare Products Regulatory Agency 2020; Pan American Health Organization (PAHO) 2020; World Health Organization (WHO) 2020c) |
| Alarm: Low inspiratory pressure. | (Pan American Health Organization (PAHO) 2020; World Health Organization (WHO) 2020c) |
| Alarm: Low/high inspiratory pressure exceeded. | (Medicines and Healthcare Products Regulatory Agency 2020) |
10 and 30 bpm. However, in the treatment of COVID-19, the adjustment value of this parameter could be above 35 bpm (Zhang et al. 2020) and, in this case, the minimum description presented by MHRA (UK) would not answer, but would be answered by other equipment. PEEP, as presented by Pedersen et al. (2020), had a higher value of 18 cmH₂O, and it was also attended to by the equipment presented as showed in Table 5.

Some attributes related to the functional part were not mentioned in any of the articles; however, it was important to characterize, for example, the need for an emergency power source. Therefore, both MHRA (UK) and AMIB (Brazil) recommended that the equipment had an operating time of 2 h (Associação de Medicina Intensiva Brasileira 2020; Medicines and Healthcare Products Regulatory Agency 2020). Table 6 identifies some points that were not found in the routines for using the eligible articles in this study. Among these points, we could include issues of alarm, monitoring, and adjustment of different parameters, such as flow, volume, and pressure, and even other ventilatory modes. It was not possible to define with the limitations of this study the real need to use all these resources for a better ventilatory practice to be used in a patient with COVID-19.

It was also noted that no references were found in the research base or the guidelines of regulatory agencies and relevant institutions on the following characteristics related to ventilator equipment:

- **Settings:**
  - Trigger mechanism, flow pattern/waveform adjustment, sigh breath function, auto 100% increase O₂ button, control panel lock.

- **Ventilation modes:**
  - Combination modes, combo mode names, active/responsive exhalation valve, time-cycled, pressure limited mode.

- **Patient alarms of continuous high pressure/occlusion, inverse IE ratio.**

- **Miscellaneous information:** output ports type (number), remote alarm/display port, reporting (vent alarms and patient status), view reports on display, possibility to save data to external media or send data via network.

- **Display:** type, size data displayed, optional equipment required for patient transport, hand-carried during transport.

- **Approved for aircraft use, MRI conditional.**

- **Power source, line power, current, internal back-up battery, recharging time, or external back-up battery, operating time, rechargeable, recharging time.

### Conclusion

In this systematic review, we found that it was possible to suggest a relationship between the clinical condition of the patient infected with SARS-Cov-2 and the type of ventilation support to be adopted.

The included studies used modes and parameters ventilatory within the specifications and recommendations of regulatory agencies and relevant institutions. There were some minor differences in recommendations between the organs, more related to the ventilatory modes and tidal volume. But some parameters, alarms, and monitoring were not defined either by the articles or by regulatory agencies and relevant institutions. Therefore, it is still incipient to deduce the basic characteristics of development and construction of mechanical ventilation equipment, since SARS-CoV-2 still has its effects on human physiology being analyzed and characterized.

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### Declarations

**Conflict of interest** The authors declare no competing interests.

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