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REVIEW ARTICLE

Outcomes associated with airway management techniques in COVID-19: narrative literature review

Desfechos associados às técnicas de manejo de via aérea na COVID-19: revisão narrativa de literatura

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ABSTRACT

Introduction: The coronavirus is a pathogen responsible for miscellaneous infections, enteric, neurological, and mainly respiratory, which can be of low to high severity. In the year 2019, in China, a new variant, SARS-CoV 2, spread, triggering a pandemic with countless human damages. In this disease, symptoms ranged from mild respiratory conditions to Severe Acute Respiratory Syndrome (SARS). Thereby, health services had to adapt to a high demand for cases that depended on careful airway management. **Objective:** this study aims to evaluate the main forms of ventilation in hospitalized COVID-19 patients, seeking to identify the main associated outcomes, such as mortality, length of hospital stay and main complications. **Methods:** We performed a narrative literature review. The research question based on the acronym Population, Intervention, Comparison and Outcomes (PICO). The Medical Subject Headings (MeSH) "airway management", "respiration, artificial", "covid-19", "survival", "length of stay" and "mortality" was used, in addition to their respective associated terms and synonyms, combined via the Boolean operators "AND", "OR" and "AND NOT". The initial search found 2058 articles for the period from March 2020 to July 2021. After cutting duplicates and applying the inclusion and exclusion criteria, 12 articles were included for analysis. **Results and Discussion:** The studies evaluated were cross-sectional, case-control, cohort and clinical trials. The types of ventilation found were, for the non-invasive (NIV), Continuous Positive Airway Pressure (CPAP), High Flow Nasal Cannula (HFNC) and face mask. Among invasive mechanical ventilation (IMV), Endotracheal Intubation (ETI) and tracheostomy stand out. The results showed that most of the negative outcomes were associated with mechanical ventilation, with studies pointing to higher mortality for invasive procedures. Among the non-invasive techniques, there were also differences in the way that CPAP reduced the need for intubation in relation to high-flow nasal oxygen therapy, in addition to shorter hospital stay and mortality. Tracheostomy was identified as necessary in up to 13% of mechanically ventilated patients, especially for those on long-term mechanical ventilation (IMV). **Conclusion:** This study found that the main forms of airway management for SARS in COVID-19 patients are NIV, with emphasis on helmet, HFNC and O2 mask, and invasive

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mechanical ventilation (IMV) with ETI and tracheostomy. The outcomes of mortality, length of stay and complications were more intense for patients on MV. However, these results must be analyzed with caution, as critically ill patients generally require more invasive procedures. The prone position was associated with better oxygenation in critically ill patients, and may be an important technique in these patients, despite not reducing mortality or length of hospital stay.

Keywords: COVID-19; Airway management; Survival; Length of stay.

RESUMO

Introdução: O coronavírus é um patógeno responsável por causar infecções de diversas naturezas, entéricas, neurológicas e principalmente respiratórias, que podem ser de baixa a alta gravidade. No ano de 2019, na China, uma nova variante, o SARS-CoV-2 se espalhou, desencadeando uma pandemia com incontáveis danos humanos. Nessa doença, os sintomas envolviam desde condições respiratórias leves até Síndrome Respiratória Aguda Grave (SRAG). Devido a isso, os serviços de saúde tiveram que se adaptar para uma demanda elevada de casos que dependiam de manejo cuidadoso de via aérea. **Objetivo:** este estudo objetiva avaliar quais as principais formas de ventilação em pacientes com COVID-19 hospitalizados, buscando identificar os principais desfechos associados, como mortalidade, tempo de permanência hospitalar e principais. **Métodos:** foi realizada uma revisão narrativa de literatura. A pergunta de pesquisa se deu a partir do acrônimo *Population, Intervention, Comparison e Outcomes* (PICO). A busca foi feita utilizando os *Medical Subject Headings (MeSH) "airway management", "respiration, artificial", "covid-19", "survival", "length of stay" e "mortality"*, além dos seus respectivos termos associados e sinônimos, combinados via os operadores boleanos *"AND"*, *"OR"* e *"AND NOT"*. A busca inicial encontrou 2.058 artigos para o período de março 2020 até julho de 2021. Após corte de duplicadas e aplicação dos critérios de inclusão e exclusão, 12 artigos foram incluídos para análise. **Resultados e Discussão:** os estudos avaliados foram analíticos do tipo transversal, caso-controle, coorte e ensaio clínico. As formas de ventilação encontrada foram, para as não invasivas (VNI), "Continuous Positive Airway Pressure" (CPAP), Cânula Nasal de Alto Fluxo e máscara facial. Entre a ventilação mecânica invasiva (VMI) destacam-se a intubação orotraqueal IOT e a traqueostomia. Os resultados demonstraram que grande parte dos desfechos negativos estiveram associados à ventilação mecânica, com os estudos apontando uma maior mortalidade para os procedimentos invasivos. Entre as técnicas não invasivas também houve diferenças, de forma que o CPAP reduziu a necessidade de intubação orotraqueal em relação à cânula nasal de alto fluxo, além de menor tempo de internação e mortalidade. A traqueostomia foi apontada como de uso necessário em até 13% de pacientes ventilados mecanicamente, sobretudo para aqueles sob ventilação mecânica invasiva (VMI) duradoura. **Conclusão:** este estudo encontrou que as principais formas de manejo de via aérea para SRAG em pacientes com COVID-19 são ventilação não invasiva (VNI), com destaque para capacete, CNAF e máscara de O2, e VMI com IOT e traqueostomia. Os desfechos de mortalidade, tempo de internação e complicações foram mais intensos para pacientes sob VMI. No entanto, esses resultados devem ser analisados com cautela, visto que pacientes graves geralmente necessitam de procedimentos mais invasivos. A posição prona foi associada com melhor oxigenação em pacientes graves, podendo ser uma técnica importante nesses pacientes.

Palavras-chave: COVID-19; Manejo de via aérea; Sobrevida; Tempo de Internação.

Introduction

The coronavirus is a pathogenic entity that has been present in human life for several years, being responsible for causing complications of various biological systems, such as enteric, neurological, and mainly respiratory, which can be from low to high severity[1]. As an example, in the last 15 years, two highly pathogenic respiratory strains have been identified, such as the severe acute respiratory syndrome coronavirus (SARS-CoV) and the Middle East respiratory syndrome coronavirus (MERS-CoV), the latter being responsible for outbreaks throughout of the last decade[1,2].

In addition, in 2019 in the city of Wuhan, China, an outbreak of cases of pneumonia of unknown cause triggered. Later, confirmed that it was a new type of coronavirus, very similar to SARS-CoV, called SARS-CoV-2, responsible for the disease COVID-19[3]. This new virus spread promptly in the region due to its high transmissibility, later spreading to several countries, resulting in a pandemic with countless global impacts and becoming a major challenge to health systems in several nations[4].

Clinically, that most patients treated for the new coronavirus had general and mild symptoms, such as fever, cough, dyspnea and fatigue. However, a small portion progressed to Severe Acute Respiratory Syndrome (SARS)[4]. Studies show that this unfavorable evolution occurs because of the host-pathogen interaction, so that both viral factors, such as greater virulence, and individual factors, such as greater response by the immune system, interfere with the risk of infection[3-5]. Besides, some groups of individuals were more subject to worse evolution, such as the elderly and those with cardiovascular, pulmonary, neoplastic and metabolic comorbidities[6-8]. In these cases, the patient present intense oxygen desaturation, pulmonary and systemic collapses, requiring emergency care and intensive therapy in a hospital environment, especially with regard to airway management, so that a large number of these patients evolve with unfavorable outcomes, such as long hospital stay, complications and mortality[9].

Thus, COVID-19 presents itself as a pathology that affects the pulmonary system, with the ability to lead many patients to respiratory dysfunction and SARS. As a result, this objective study evaluates the main forms of ventilation in hospitalized patients with COVID-19, seeking to identify the main associated complications, such as mortality, length of hospital stay and main complications.

Methods

This is a narrative literature review, in which the research question elaborated based on the acronym Population, Intervention, Comparison and Outcomes (PICO). However, as this work does not aim to compare specific interventions, the research question only involved population, intervention and outcomes. In this context, the population studied was COVID-19 patients, the intervention was airway management, and the primary outcomes evaluated were death and length of hospital stay. Secondary outcomes were technical complications.

The search was performed using the Medical Subject Headings (MeSH) "airway management", "respiration, artificial", "COVID-19", "survival", "length of stay" and "mortality", in addition to their respective associated terms and synonyms, combined via the boolean operators "AND", "OR" and "AND NOT". The analysis and inclusion flowchart of the studies followed the PRISMA model (Figure 1). The inclusion criteria defined were direct analysis of survival, mortality or length of stay in COVID-19 patients undergoing mechanical ventilation, cross-sectional analytical studies, case-control, cohort and clinical trials, from the last two years. Exclusion criteria were studies with patients under 18 years of age, incomplete articles, descriptive analysis studies, absence of keywords and synonyms in the title and abstract, studies that evaluated airway control in non-COVID-19 patients, studies in non-hospitalized patients, small sampling (n<50) and publications in languages other than English and Portuguese.

The search string applied to PubMed, Cochrane and "Biblioteca Virtual em Saúde (BVS)" platforms. Initially, we found 2058 articles from March 2020 to July 2021. Filters was applied for type of studies and language. After filtering and removing duplicates using the Mendeley, 494 articles obtained. In sequence, the works of this search were exported to Parsifal software, through which the authors read the titles and abstracts, applying the inclusion and exclusion criteria. After this selection, 48 studies were filtered. Subsequently, the full reading of the articles, with new 36 exclusions, resulted in a final selection of 12 articles.

Results

Of the 12 articles evaluated, only one was randomized clinical trial (RCT), while the others corresponded to observational studies. Of these, 6 were prospective cohorts and 6 studies were retrospective, such as case-controls and historical cohort. Eight studies were multicenter, while the rest were local, regional or national. Table 1 brings a summary of the evaluated articles.

Among the Non-Invasive Ventilation (NIV) techniques, the ones found were the CPAP helmet, the face mask and the high flow nasal cannula (HFNC). Among the Invasive Mechanical Ventilation (IMV) techniques, those described were Endotracheal Intubation (ETI) and tracheostomy. In addition, some studies evaluated special situations, such as the prone position.

The main outcomes evaluated for articles that studied non-invasive techniques were general mortality, length of hospital stay and the need for invasive procedures after poor

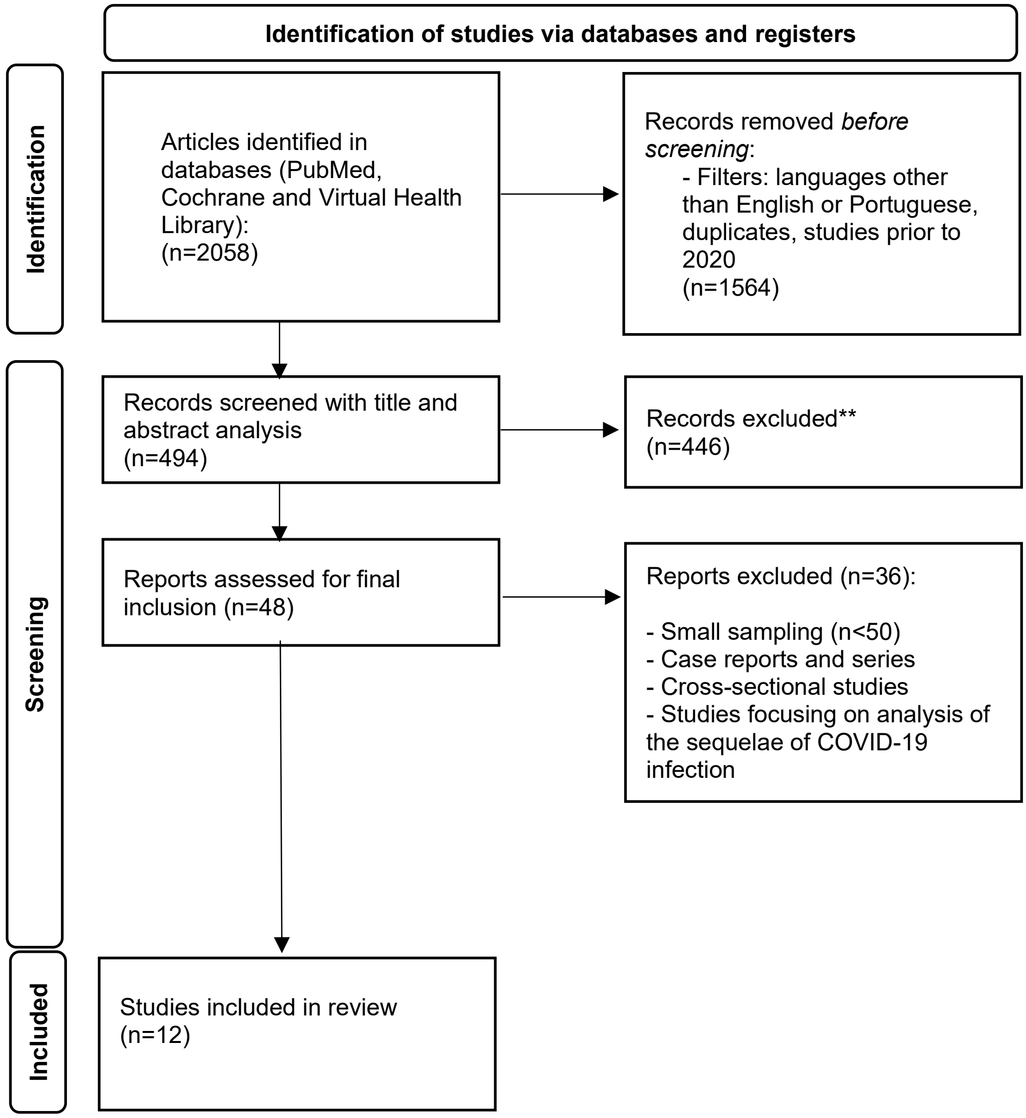

Figure 1. PRISMA flowchart for analysis of included studies.

clinical evolution. Regarding invasive procedures, the main outcomes were mortality and length of hospital stay. The analysis of risk factors for worse prognosis was also present.

HFNC and oxygen helmet

The only RCT found sought to compare helmet with HFNC, involving 109 patients[10]. Of these, 54 received a helmet and 55 a HFNC. The primary objective was to compare the number of days until the end of ventilatory support, in which no significant difference was observed between the groups (20 days in the helmet group versus 18 days in the HFNC group, p=0.26). The same occurred for hospital mortality, with a rate of 24% in the helmet group and 25% in the HFNC group. However, the evolution to ETI was significantly lower for the helmet group (30% versus 51%; p=0.03)[10].

A cohort study of 136 patients also compared HFNC with oxygen helmets. Fifty-eight patients received the helmet, and 78 the HFNC – this was the control. it was observed a higher mortality in the control group, but with no significant difference between the two, 69.2% versus 62.1% CI 0.73 (0.36-1.5). Nevertheless, as in the RCT, the helmet group showed a lower rate of evolution to IMV with an average improvement of 8.8% in SaO_2 (p<0.001)[11].

A prospective cohort by Celejewska-Wójcik et al. (2021)[12] aimed to assess the mortality rate as a primary outcome in patients undergoing HFNC. The value found for 30-day mortality was 30.2% (35 of 116 patients). It is noteworthy that 51 patients (44% of the sample) required ETI after HFNC, and among them the mortality was 64.7%. In this study, the median number of hospitalization days for the sample was 20 days for the ward and 10 days for the Intensive Care Unit (ICU). A retrospective cohort study of 272 patients with HFNC found an average of 14 days of ICU stay, and mortality of 18% for this procedure[13].

Table 1. Assessed studies, method and main results.

Author	Method	Analysis	Results
Grieco et al. (2021)[10]	Randomized Clinical Trial	HFNC x Helmet NIV	**1- Number of days of ventilation:** 20 helmet group x 18 days in the HFNC group (p=0.26) **2- Hospital mortality:** 24% in the helmet group x 25% in the HFNC group **3- Evolution to ETI:** 30% helmet x 51% HFNC (p=0.03)
Dayya et al. (2021)[11]	Prospective cohort	HFNC x Helmet NIV	**1- Hospital mortality:** HFNC 69.2% x 62.1% Helmet OR 0.73 95%CI (0.36-1.5) **2- Evolution to VMI:** Helmet had a lower rate of evolution for IMV with an average improvement of 8.8% in SaO_2 (p<0.001)
Celejewska-Wójcik et al. (2021)[12]	Prospective cohort	Mortality rate in patients under HFNC Evolution ratio for ETI	**1- Mortality:** 30.2% in 30 days **2- Evolution to ETI:** 44% of the sample **3- Median days of hospitalization:** 20 days ICU, 10 days ward
Chandel et al. (2021)[13]	Retrospective cohort	Average length of stay and for patients under HFNC	**1- Mean ICU stay** 14 days **2- HFNC associated mortality** 18% mortality
Roedl et al. (2021)[14]	Retrospective cohort	Mortality and length of stay (LS) in the ICU: IMV x NIV	**1- Mortality** **- General: n=78 (34.8%)** - IMV: n=74 (33.03% of the sample and 94.7% of deaths) - NIV: n=4 (1.7% of the sample and 5.3% of deaths) **2- LS ICU** VMI 18 days x NIV 3 days
Wang et al. (2020)[15]	Retrospective cohort	Hospital Mortality: IMV x NIV	Higher hospital mortality associated with IMV compared to NIV (Hazard Ratio - HR: 2.95; 95% CI, 1.40–6.23; p=0.005)
Walker et al. (2020)[16]	Case control	Mortality and length of stay (LT) for CPAP, nasal oxygen and IMV	**1- Mortality rate** - CPAP: 46.7% - Nasal oxygen: 33% - IMV: 41.2% **2- IT** Median of 7 days NIV x 24 days NIV (p<0.001)
Ahmed et al. (2021)[17]	Retrospective cohort	Mortality and cannula time in tracheostomy	**1- Average cannula time** 37 days among non-survivors and 50 days among survivors
Chao et al. (2020)[18]	Prospective cohort	Mean length of stay in tracheostomy	**1- Average length of hospital stay** 11.8 days ± 6.9 days
Martin-Villares et al. (2021)[19]	Prospective cohort	Surgical vs percutaneous tracheostomy:	**1 - Median length of stay** 12 days (4-42 days) **2- General mortality** 23.7% Complication rate and mortality compared between groups showed no significant difference
Langer et al. (2021)[20]	Prospective cohort	Pronation response in the PaO_2/FiO_2 ratio	Significant increase in the PaO_2/FiO_2 ratio, with a mean value of 158 mmHg for PP versus 98 mmHg for baseline pre-pronation and 128 for re-supination (p<0.001)
Taboada et al. (2021)[21]	Prospective cohort	Assessed of IMV x NIV complications	**1- Main complications associated with MV:** pneumothorax, shock, pulmonary embolism, acute kidney injury, reintubation, thrombotic events, intestinal bleeding and oxygen desaturation with cardiac arrest **2- Main complications associated with NIV** Evolution to VMI

Invasive mechanical ventilation (IMV) *versus* non-invasive ventilation (NIV)

Some articles compared more than two concomitant techniques. Roedl et al. (2021)[14] compared IMV with NIV in a study of 224 individuals, in which 167 used IMV, 31 used NIV and 26 used HFNC. Overall mortality was 78 patients, among which 74 (94.7%) belonged to the IMV group. Likewise, the length of stay in the ICU was also longer for invasive mechanically ventilated patients, with an average of 18 days versus 3 days for the unified NIV and HFNC group[14]. Another study with a large sample brought important information, showing that the greater chances of hospital death were associated with the need for IMV in relation to NIV (Hazard Ratio - HR: 2.95; 95% CI, 1.40–6.23; p=0.005)[15].

Case-control of 294 patients evaluated CPAP, nasal oxygen therapy and mechanical ventilation[16]. In that study, the mortality rates for CPAP, nasal oxygen and IMV were, respectively, 46.7%, 33% and 41.2%. As for the length of stay, there was no significant difference between the NIV groups, but with a difference between this group and the IMV group (median of 7 days *vs* 24 days, respectively, X^2 p<0.001).

Tracheostomy

Tracheostomy was described in 3 studies. A cohort by Ahmed et al. (2021)[17] with 64 tracheostomized patients found a 30-day mortality rate of 33%[17]. Mean cannula time was 37 days among non-survivors and 50 days among survivors. Along the same lines, Chao's group (2020)[18] evaluated 53 tracheostomies, finding a mean hospital stay of 11.8 days ± 6.9 days, with a lower mortality rate, of only 11.3%[18].

A large cohort of 1.890 patients compared surgical and percutaneous techniques to assess weaning time, mortality, complications and length of stay.[19] There were 1461 surgical and 429 percutaneous tracheostomies. The median length of stay was 12 days (4-42 days), and mortality was 23.7%. The complication rate and mortality compared between the groups showed no significant difference (p>0.05).

Prone position

The prone position (PP) was reported as a way to improve oxygenation in COVID-19 patients. This intervention demonstrated in a multicenter cohort of 1057 participants, in which 648 received PP[20]. In that study, the authors evaluated response to oxygen according to the PaO_2/FiO_2 ratio, which was considered positive when there was an increase ≥20 mmHg during pronation in relation to baseline values in the supine position. In general, there was a significant increase in the PaO_2/FiO_2 ratio, with a mean value of 158 mmHg for PP versus 98 mmHg for baseline pre-pronation and 128 for resupination (p<0.001). However, no association was found with improvement in lung compliance or ventilatory ratio. In addition, higher mortality rates, duration of mechanical ventilation and hospital stay were observed in the group submitted to PP, mainly due to the more severe baseline status of these patients.

Complications

The main complications varied according to the type of study. For those investigating non-invasive procedures, the main one was the need to use mechanical ventilation[10,11,22]. One study pointed out acute kidney injury, need for dialysis and infections as complications of patients undergoing HFNC, due to the lower effectiveness of NIV to delay the progression of infection and respiratory compromise by COVID[13]. As for the articles that addressed mechanical ventilation, the main complications found were pneumonia associated with mechanical ventilation, pneumothorax, shock, pulmonary embolism, acute kidney injury, reintubation, thrombotic events, intestinal bleeding and oxygen desaturation with cardiopulmonary arrest[14,21]. Regarding tracheostomies, the complications described were bleeding, intraoperative pneumothorax, mucous plug, dislodged tube, air leakage, and cellulitis[17-19].

Discussion

The results analysis showed that most of the negative results remained associated with mechanical ventilation. In this sense, comparative studies[14,16] of NIV with IMV pointed to higher mortality for invasive procedures. However, this comparison, without analysis of the type of population studied, does not allow confirmation that MV causes worse declines in relation to NIV, because patients submitted to MV tend to present several risk factors that lead to a more severe condition[23]. These factors were hypertension, diabetes, chronic kidney disease, obesity and smoking were conditions found in most critically ill patients participating in the studies[11-22].

Thus, higher mortality and longer hospital stay may be associated more with the patient's condition than with the technique itself. This same interpretation is given by a review that identified that some risk factors for MVI in a condition of respiratory failure, such as chronic cardiovascular and pulmonary diseases and obesity, subjected the individual to a greater probability of mortality, complications and prolonged hospitalization time[24]. Furthermore, laboratory markers such as d-dimer, LDH, CRP, CRP, ferritin, creatinine, TGO, TGP and bilirubin were also identified as predisposing factors for major complications[10,14-16,20,22].

Our results also show that there may be significant differences in results among non-invasive techniques. In brief, the oxygen helmet reduced the need for endotracheal intubation in relation to high-flow nasal oxygen therapy[10,11]. Although the studies did not demonstrate significant differences between mortality and length of hospital stay for helmet and HFNC, it is believed that, because training reduces the need for ETI, it may be associated with lower mortality and reduced hospital stay. Nonetheless, to evaluate this result, larger studies are needed, involving more patients, which would provide a sample capable of providing reliable results Stil, supporting our results, the review by Pedersen and Vahlkvist (2017)[25] showed that CPAP is related to lower mortality when compared to high-flow oxygen therapy in acute viral bronchiolitis in children.

Another approach we identified was tracheostomy, a procedure required in up to 13% of mechanically ventilated ICU patients[26]. This procedure has some indications for use, the main one being the need for long-lasting mechanical respiration. This can facilitate weaning and minimize the complications of a prolonged ETI[27,28]. In this context, there is a debate about the best form of tracheostomy in SARS, percutaneous or surgical, late or early. In the literature, there seems to be no supremacy of one technique over the other, as well as for the ideal performance time[29,30]. This is consistent with our result, in which the studies considered did not find changes in mortality and complication rates[19,20].

More severe patients may also benefit from the prone position as an additional measure to improve pulmonary perfusion[31]. The study we included, one of the largest in our review, found this association[20]. Here, it is worth considering that prone patients had more severe disease. Therefore, mortality, length of stay and invasive ventilation were higher for the PP group. Meanwhile, in these critically ill patients, there was a significant improvement in pulmonary perfusion, showing that pronation can be an alternative to improve the oxygenation index in this patient profile.

We emphasize that our study has some limitations, the main one related to the small sample number of individuals in some studies. In addition, only one study was Randomized Clinical Trial, while the others were observational. This can reduce the level of evidence and signal that more work needs to be done for more robust and reliable data. Despite this, our review gathers valuable information that can be used to assist in the management of airway in patients with COVID-19.

Conclusion

In summary, we found that the main forms of airway management for SARS in COVID-19 patients are NIV, with emphasis on helmet, HFNC and O_2 mask, and MVI with OTI and tracheostomy. The outcomes of mortality, length of stay and complications were more prevalent in patients on MV. However, these results should be analyzed with caution, as critically ill patients generally require more invasive procedures. Therefore, the use of one technique over another must be done according to the clinical needs of each patient.

Author's Contribution

We describe contributions to the papers using the taxonomy (CRediT) provided above:

Conceptualization, Investigation, Methodology, Visualization & Writing – review & editing: LDPM; AAGMC; VAC; ESAC; LCM; ACJSR. *Project administration, Supervision & Writing – original draft:* LDPM; ADFN. Validation & Software: LDPM; VDRC; ADFN. *Data curation & Formal Analysis:* LDPM; VDRC; ADFN.

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