The effect of Pressure- or Volume- controlled ventilation on inflammatory factors of patients undergoing surgery with the novel coronavirus (COVID-19) pneumonia: protocol for a systematic review and meta-analysis

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Protocol

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Abstract

Objective During the COVID-19 pandemic, some patients with novel coronavirus pneumonia may have concurrent disease that must be accepted surgery. However, the extensive inflammatory response existed in this population, especially in the lungs. And various ventilation could affect the inflammation of lungs. Therefore, how to choose the ventilation mode to reduce the effect of mechanical ventilation on inflammation is an important clinical practice. We aim to investigate the effect of different ventilation modes on inflammatory factor levels of patients undergoing surgery with COVID-19 through this systematic review and meta-analysis.

Methods and analysis This systematic review and meta-analysis have been registered in the International Prospective Register of Systematic Reviews (PROSPERO). The PubMed, Embase via Ovid, Chinese Biological Medical Database (CBM), China National Knowledge Infrastructure (CNKI), the Cochrane Central Register of Controlled Trials (CENTRAL) will be searched from inception to date to find relevant studies. In addition, the relevant literature was also hand-searched. Two searchers independently selected the studies, extracted data and assessed the quality of studies included. The Review Manager 5.4 software (The Cochrane library, Oxford, England) will be used for data synthesis and meta-analysis. Continuous variables were embodied by Weight Mean Differences with 95% confidence intervals (CI). Dichotomous outcomes were embodied by Odds ratio with 95%CI.

Ethics and dissemination Ethical approval is not required because the data was collected from the published studies. Finally, the results of this systematic review will be published in a peer-reviewed journal.

PROSPERO registration number CRD42021251937

Introduction

From the end of December 2019 to now, more and more patients have been diagnosed with novel coronavirus (COVID-19) pneumonia, and this epidemic was not limited in the place, Wuhan, China, and caused a global pandemic[1, 2]. Till November 2020, there were more than 8 million cases in India, and it has become one of the countries which had the fastest increasing speed of COVID-19 infection for the terrible prevention and control strategy[3, 4]. Therefore, it is a challenge for all countries, especially the poor, to manage and control the COVID-19 infection, because of the shortage of medical resources[5].

Patients with novel coronavirus pneumonia would present various clinical manifestations such as fever, cough, dyspnea, and pain, et. al[6]. And in this population, they had an apparent inflammatory reaction. For example, IL-1 β , IL-6, IL-8 was high, but the IL-10 is low[7]. In patients who suffered from acute respiratory distress syndrome, inflammation seriously increases the injury of different organs, especially the lungs [8]. The COVID-19 infection was a massive hit to people's health, and simultaneously these patients might also suffer from another acute disease that needs to be treated by surgery, such as acute surgical abdomen, and it could be a considerable challenge to manage[9]. In the perioperative period,

anesthesiologists were among the most critical roles to manage patients undergoing surgery, and the management of the respiratory is the most critical step[10]. The previous studies had found that the mode of ventilation would affect the concentration of inflammatory factors, and pressure-control ventilation might decrease the level of tumor necrosis factor (TNF)- α and interleukin (IL)-6 and also increase the level of IL-10 compared with volume-controlled ventilation[11]. However, another study revealed no difference in inflammatory factor levels between volume- and pressure-controlled ventilation. So, it is unclear whether the mode of ventilation could influence the level of inflammatory marker. However, these factor levels are important for surgical patients' recovery, especially the persons with novel coronavirus pneumonia who have a high level of inflammation.

Therefore, to the anesthesiologists' best to minimize the influence of anesthesiology on the inflammatory level is significantly essential. So, it is significant to investigate the effect of various ventilation modes on inflammatory factors of surgical patients with COVID-19. Additionally, till now, no systematic review and meta-analysis are examining the influence of the ventilation approach on inflammatory marker levels of patients undergoing surgery with COVID-19. Therefore, we will qualitatively and quantitatively investigate the effects of pressure- or volume-controlled ventilation on patients' inflammatory factors with novel coronavirus pneumonia in this systematic review and meta-analysis.

Methods

This protocol of systematic review and meta-analysis was conducted in line with the Preferred Reporting Items for Systematic Reviews and Meta-analyses Protocols (the PRISMA-P) [12]. The PROSPERO registration number is CRD42021251937. For the nature of this article, no informed consent of patients was needed.

Literature search

The PubMed, Web of Science, Embase via Ovid, Chinese Biological Medical Database(CBM), China National Knowledge Infrastructure(CNKI), the Cochrane Central Register of Controlled Trials (CENTRAL) will be searched by two reviewers independently to full access to relevant research from inception to date. In addition, the relevant pieces of literature were also hand-searched. Studies concerning the effects of ventilation mode for patients' inflammatory factor levels with COVID-19 in the surgery period will be brought into this meta-analysis, including randomized controlled trials (RCTs), controlled clinical trials (CCTs), prospective and retrospective comparative cohort studies, cross-sectional researches and observational researches. The search terms included 'pressure-controlled ventilation' and 'volume-controlled ventilation' and 'COVID-19' or 'novel coronavirus pneumonia' or 'SARS-CoV-2', and 'inflammation', and the detailed search strategy of PubMed is presented in Table 1. There are no language restrictions.

Table 1: search strategy of PubMed

Search	Query
#1	"covid 19"[MeSH Terms]
#2	"covid 19"[All Fields] OR "covid 19"[MeSH Terms] OR "covid 19 vaccines"[All Fields] OR "covid 19 vaccines"[MeSH Terms] OR "covid 19 serotherapy"[All Fields] OR "covid 19 serotherapy"[Supplementary Concept] OR "covid 19 nucleic acid testing"[All Fields] OR "covid 19 nucleic acid testing"[MeSH Terms] OR "covid 19 serological testing"[All Fields] OR "covid 19 serological testing"[MeSH Terms] OR "covid 19 testing"[All Fields] OR "covid 19 testing"[MeSH Terms] OR "sars cov 2"[All Fields] OR "sars cov 2"[MeSH Terms] OR "severe acute respiratory syndrome coronavirus 2"[All Fields] OR "ncov"[All Fields] OR "2019 ncov"[All Fields] OR (("coronavirus"[MeSH Terms] OR "coronavirus"[All Fields] OR "cov"[All Fields]) AND 2019/11/01:3000/12/31[Date - Publication]) OR ("covid 19"[MeSH Terms] OR "covid 19"[All Fields] OR "covid 19 virus disease"[All Fields]) OR ("covid 19"[MeSH Terms] OR "covid 19"[All Fields] OR "covid 19 virus infection"[All Fields]) OR ("covid 19"[MeSH Terms] OR "covid 19"[All Fields] OR "2019 ncov infection"[All Fields]) OR ("covid 19"[MeSH Terms] OR "covid 19"[All Fields] OR "coronavirus disease 19"[All Fields]) OR ("covid 19"[MeSH Terms] OR "covid 19"[All Fields] OR "2019 novel coronavirus disease"[All Fields]) OR ("covid 19"[MeSH Terms] OR "covid 19"[All Fields] OR "2019 novel coronavirus infection"[All Fields]) OR ("covid 19"[MeSH Terms] OR "covid 19"[All Fields] OR "2019 ncov disease"[All Fields]) OR ("covid 19"[MeSH Terms] OR "covid 19"[All Fields] OR "covid19"[All Fields]) OR ("covid 19"[MeSH Terms] OR "covid 19"[All Fields] OR "coronavirus disease 2019"[All Fields]) OR ("covid 19"[MeSH Terms] OR "covid 19"[All Fields] OR "sars coronavirus 2 infection"[All Fields]) OR ("covid 19"[MeSH Terms] OR "covid 19"[All Fields] OR "sars cov 2 infection"[All Fields]) OR ("covid 19"[MeSH Terms] OR "covid 19"[All Fields] OR "covid 19 pandemic"[All Fields])
#3	#1 or #2
#4	"pressure-controlled"[All Fields] AND ("ventilated"[All Fields] OR "ventilates"[All Fields] OR "ventilating"[All Fields] OR "ventilation"[MeSH Terms] OR "ventilation"[All Fields] OR "ventilate"[All Fields] OR "ventilations"[All Fields] OR "ventilator s"[All Fields] OR "ventilators, mechanical"[MeSH Terms] OR ("ventilators"[All Fields] AND "mechanical"[All Fields]) OR "mechanical ventilators"[All Fields] OR "ventilator"[All Fields] OR "ventilators"[All Fields] OR "ventillation"[All Fields])
#5	"volume-controlled"[All Fields] AND ("ventilated"[All Fields] OR "ventilates"[All Fields] OR "ventilating"[All Fields] OR "ventilation"[MeSH Terms] OR "ventilation"[All Fields] OR "ventilate"[All Fields] OR "ventilations"[All Fields] OR "ventilator s"[All Fields] OR "ventilators, mechanical"[MeSH Terms] OR ("ventilators"[All Fields] AND "mechanical"[All Fields]) OR "mechanical ventilators"[All Fields] OR "ventilator"[All Fields] OR "ventilators"[All Fields] OR "ventillation"[All Fields])
#6	#4 or #5
#7	"inflammation"[MeSH Terms] OR "inflammation"[All Fields] OR "inflammations"[All Fields] OR "inflammation s"[All Fields] OR (("inflammatories"[All Fields] OR "inflammatory"[All Fields]) AND ("response"[All Fields] OR "responses"[All Fields] OR "responsive"[All Fields] OR "responsiveness"[All Fields] OR "responsivenesses"[All Fields] OR "responsives"[All Fields] OR "responsivities"[All Fields] OR "responsivity"[All Fields]))
#8	#3 and #6 and #7

Eligibility Criteria

Type of study design

All relevant studies, such as RCTs, CCTs, prospective and retrospective comparative cohort studies, cross-sectional researches, and observational researches, will be covered in this meta-analysis. Due to the deficiency of original trials, we try our best to find out as many relevant studies as possible.

Participants

The patients with COVID-19 who have been controlled breathing through pressure- or volume-controlled mode in the surgery will be involved. Because the number of concerning studies is relatively small, we do not restrict the population's age. Adult and pediatric patients will be included in this meta-analysis. The studies from various countries will be included in the world.

Interventions

The interventions will be various ventilation modes, including Pressure-controlled ventilation and Volume-controlled ventilation during the surgery period.

Outcomes

The primary outcome is the inflammatory factor levels in 3h,6h,12h, and 24h after surgery, including IL-6, IL-8, TNF- α , and IL-10. And the secondary outcomes are as follows: postoperative oxygenation index, blood oxygen saturation, serum creatinine concentration, incision infection rate, and hospitalization time.

Study Selection And Data Collection

Two searchers will independently select the studies. If some discrepancies exist between the searchers, further discussion will be done with a senior reviewer to solve this problem. After removing the duplicates, we will assess the preliminary quality of studies according to the title and abstract. And then, we will do the final assessment by reading the full text. The selection flow gram is presented in Fig. 1. A standard collection form will be adopted to extract the data by two reviewers independently. Any discrepancies will be solved by another senior reviewer. The extracted data including first author, date of publication, sample size, patient characteristics, ASA physical status, type of surgery, type of study, ventilation mode, surgery and anesthesia time, postoperative laboratory results, inhaled oxygen concentration after surgery, patients' number of incision infection, and length of hospitalization. For the missing data, we will contact the author to get it.

Risk-of-bias Assessment And Quality Assessed

Two tools would be used to evaluate the quality of studies included. The randomized controlled trials were evaluated by Cochrane's risk-of-bias tool according to the following domains: bias arising from the randomization process, bias due to deviations from intended interventions, bias owing to missing outcome data, bias from the measurement of the outcome, bias from the selection of the reported result[13]. And for the non-randomized studies, we will use the Newcastle-Ottawa Scale (NOS) to evaluate the bias, including subjects selection, study comparability, and outcome measurement [14]. According to the tool of assessing the risk of bias, the decisions could be 'Low', or 'High' risk of bias, or express 'Some concerns'. The risk of bias would be assessed by two searchers independently. And the quality of

evidence about the studies included was evaluated with the Grading of Recommendations, Assessment, Development, and Evaluation (GRADE) criteria[15].

Data synthesis and statistical analysis

The Review Manager 5.4 software (The Cochrane library, Oxford, England) was used for data synthesis and meta-analysis. Continuous and dichotomous outcomes were embodied by Weight Mean Differences [WMD, 95% confidence intervals (CI)] and odds ratios [OR, 95% CI], respectively. The heterogeneity would be tested with the I^2 index ($I^2 > 50\%$ indicated significant heterogeneity) [16]. If data had significant heterogeneity, a random effect model would be used. Without obvious heterogeneity, a fixed-effect model would be applied.

Subgroup analysis, sensitivity analysis, and publication bias assessment

If significant heterogeneity existed, subgroup analysis would be done depending on the severity of COVID-19 and surgery type. Subgroup analysis was executed when there were at least two studies in each subgroup. Sensitivity analysis was performed by repetitively taking away one study at one time. If the final pooled results did not change after removing one study, the meta-analysis would be considered to be reliable and stable[17]. Funnel plot asymmetry was used to detect publication bias[18].

Ethics And Dissemination

Ethical approval is not required for the reason that the data was collected from the published reports. Finally, the results of this systematic review will be published in a peer-reviewed journal.

Discussion

As far as we know, this is the first meta-analysis to examine the effects of Pressure- or Volume-controlled ventilation on patients' inflammatory factor levels with novel coronavirus pneumonia who have experienced surgery. It is crucial for patients who have undergone surgery with COVID-19 to select a proper ventilation mode during the anesthesia period [19]. In this population, the extensive inflammatory response is a significant feature, especially the location of the lungs, so it is vital to reduce this response by using a fit ventilation method. However, it is uncertain whether ventilation mode could influence the inflammatory marker levels in patients undergoing surgery with coronavirus pneumonia due to limited original searches. This is the significant problem which we concern. And also, there is the main limitation in our meta-analysis for the insufficiency of RCTs, which may reduce the strength of evidence.

Declarations

Ethics approval and consent to participate

Not applicable

Consent for publication

Not applicable.

Availability of data and materials

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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Authors' contributions

BJ and MYC designed this review and made the search strategy. BJ and MYC completed the literature search, data collection. BJ and XL will perform the data synthesis and analysis, and BJ was the major contributor to write the protocol draft writing, JL and CC revised the manuscript critically. All authors have read and approved the final version.

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Not applicable

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Figures

Figure 1

The flow diagram of literature search and selection

Supplementary Files

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