The effect of driving pressure-guided ventilation strategy on the patients with mechanical ventilation: a meta-analysis of randomized controlled trials

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Abstract. – OBJECTIVE: The aim of this study was to evaluate the effect of driving pressure (DP) guided ventilation strategy on the patients with mechanical ventilation in the hospital.

MATERIALS AND METHODS: The articles published in PubMed, the Cochrane Library, the China National Knowledge Information (CNKI), Wei Pu, Wan Fang database and Web of Science from inception to September 2021 were retrieved. The Q test and the I^2 statistic were used to assess statistical heterogeneity. Risks ratios (RR) with 95% confidence intervals (CI) were calculated for mortality.

RESULTS: Seven studies (n=1,405 patients) were included. Five studies reported an adjusted Risk Ratio (RR) of mortality. Compared with the control group, the DP guided ventilation group was associated with a decreased mortality (RR 0.56; 95% confidence interval [CI], 0.39-0.79; p=0.001; I^2 = 23%) using a fixed-effects model without significant heterogeneity. The control group had significantly higher driving pressure level than DP guided group (MD -3.03, 95%CI, -5.72 – -0.34, I^2=100%, p=0.03); PaO_2/FiO_2 was significantly higher in DP guided group than in control group (MD 43.37; 95%CI, 12.58-74.15; I^2=97%, p=0.006). There was no statistically significant difference in respiratory compliance, complications, platform pressure, duration of mechanical ventilation and the length of hospital stay between the DP guided group and the control group.

CONCLUSIONS: The results suggested that the driving pressure guided ventilation strategy could decrease the mortality and increase oxygenation index (OI). However, further high-quality randomized controlled trials (RCTs) are needed to verify the impact of driving pressure on mechanically ventilated patients.

Key Words:
Driving pressure, Mechanical ventilation, Ventilator-induced lung injury (VILI), Meta-analysis.

Abbreviations

DP: driving pressure; CNKI: China national knowledge information; RR: risk ratio; CI: confidence interval; OI: oxygen index; RCTs: randomized controlled trials; VILI: ventilator-induced lung injury; MV: mechanical ventilation; PPC: postoperative pulmonary complications; VT: tidal volume; ICU: intensive care unit; PEEP: positive end-expiratory pressure; ECMO: extracorporeal membrane oxygenation; CRS: compliance of the respiratory system; LPV: lung protective ventilation; COVID-19: Coronavirus disease 2019; PRISMA: Preferred Reporting Items for Systematic Reviews and Meta-Analyses.

Introduction

In the United States, more than 4 million patients are admitted to an ICU each year, about 40% of those patients receive invasive mechanical ventilation (MV) at any time[1]. Mechanical ventilation is an essential form of life support for critically ill patients or perioperative patients and Coronavirus disease 2019 (COVID-19) patients etc., because it can improve oxygenation and maintain ventilation, reduce respiratory muscle effort, and recruit

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alveoli[2]. However, if the ventilator parameters are unreasonably set, it can not only aggravate lung injury, but also cause ventilator-induced lung injury (VILI) and affect the patient's prognosis. Although the lung protective ventilation strategy which maintains low tidal volume (V_T) and the optimal positive end expiratory pressure (PEEP) can reduce the lung damage, it is unclear how to minimize VILI through adjustment of various parameters including V_T, plateau pressure, driving pressure, and PEEP[3]. After a publication by Amato et al[4], driving pressure has attracted much attention. Driving pressure during mechanical ventilation is directly related to stress forces in the lungs, which also represent the V_T corrected by the patient's static compliance of the respiratory system (C_{RS})[5]. A retrospective study by Yildirim et al[6] on patients with COVID-19, higher driving pressure was found to be associated with higher mortality. Recent reports[4] have also confirmed that high driving pressure is usually strongly associated with higher mortality rates and more postoperative complications among the surgical patients[7]. Baedorf Kassis et al[8] research confirmed that treatment strategies with lower driving pressure could be associated with reduced mortality. Thus, it can be inferred that driving pressure is of utmost importance in VILI[9]. Chiumello et al[10] thought that setting the tidal volume by targeting driving pressure might better protect the lungs in critically ill patients. The driving pressure guided ventilation strategy may become a new ventilation strategy for mechanically ventilated patients. However, it remains to be determined whether this method is a better way to set ventilation strategies[11]. Therefore, in this meta-analysis, we investigated the effect of driving pressure-guided ventilation strategy for the patients who received mechanical ventilation.

Materials and Methods

Search Strategy

The study complied with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement[12]. We systematically searched following databases (PubMed, the Cochrane Library, CNKI, Wei Pu, Wan Fang database and Web of Science) from inception to September 2021. A basic search was performed using the following Subject terms and Synonyms: "driving pressure" AND "Respiration, Artificial" (with related synonyms: Respirations, Artificial; Artificial Respiration; Artificial Respirations; Mechanical Ventilations; Ventilations, Mechanical; Ventilation, Mechanical; Mechanical Ventilation). Two investigators (Y. Li and Q. Zhang) conducted the literature search study selection, data extraction, and quality evaluation independently. When there was disagreement between the two authors, we discussed until consensus. No language restriction was applied for article selection.

Inclusion and Exclusion Criteria

Studies were included based on the following PICOS criteria: 1. Participants: patients with MV aged ≥ 18 years; 2. Study type: randomized controlled trials (RCTs); 3. Intervention group: driving pressure guided ventilation strategy; 4. Comparison group: lung protective ventilation (LPV) strategy; 5. Outcome: mortality was the primary outcome.

Pregnant females, animals' experiments, non-randomized controlled trials, reviews, case reports, unrelated intervention and the duplication studies were excluded.

Quality Assessment

Two authors (Y. Li and Q. Zhang) evaluated the quality of the included studies. If opinions differed, further discussions were held until a consensus. For the assessment of methodologic quality and risk of bias, we evaluated each included study according to the Cochrane risk-of-bias instrument, it included that random sequence generation (selection bias), allocation concealment (selection bias), blinding of participants and personnel (performance bias), blinding of outcome assessment (detection bias), incomplete outcome data (attrition bias), selective reporting (reporting bias) and other bias. The risk bias graph (Figure 1) and summary (Figure 2) were generated by choosing low risk bias, unclear risk bias or high-risk bias. Green represents low risk of bias, yellow represents unclear risk of bias, and red represents high risk of bias.

Statistical Analysis

RevMan 5.4 software (Review Manager Computer program, The Cochrane Collaboration, Copenhagen) was used for all statistical analyses. We used the Q test and the I^2 statistic to assess statistical heterogeneity[13]. If the outcome of heterogeneity was low, as defined by an $I^2 < 50\%$ or/and $p>0.1$, we used the fixed-effects models to synthesize results. If heterogeneity was high, as indicated by an I^2 statistically greater than 50% and $p<=0.1$, we used the random-effects models

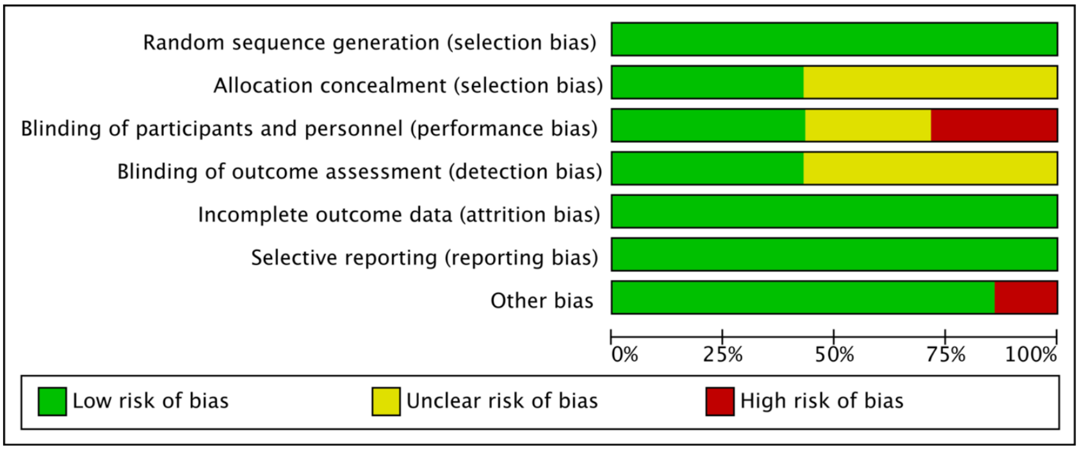

Figure 1. The risk of bias graph.

to synthesize results. We performed the analyses using the fixed-effects models and random-effects for dichotomous and continuous data, respectively. For the data shown as medians and interquartile ranges (IQRs), medians and IQRs were converted to mean and standard deviations to obtain pooled RRs and SMDs[14]. A p-value<0.05 was considered statistically significant. Funnel plot was created for the mortality. We used RevMan 5.4 software to draw funnel plot to assess publication bias, with the effect size RR as the abscissa and the reciprocal 1/SE (logRR) of the effect size against the standard error of the value as the ordinate. The scale for the abscissa was indicated by antilog, and the scale for the ordinate was indicated by SE (logRR).

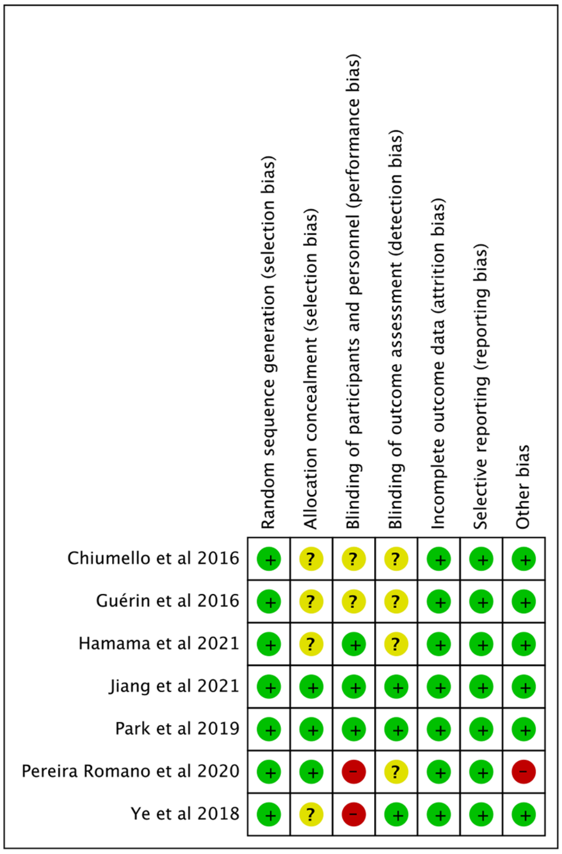

Figure 2. The risk of bias summary.

Results

The prime search confirmed 531 articles from PubMed, 237 from the Cochrane Library, 782 from Web of Science, 58 from CNKI, 17 from Wei Pu and 71 from Wan Fang Database. After excluding 1,602 articles which included reviews, animal experiments, non-adult trials, case reports, irrelevant studies based on title and abstracts, 94 articles were screened; after removing 17 duplicates by inspection of the title and author, 77 articles were subsequently reviewed by reading the full text; finally, we included data from seven randomized controlled trials[10,15-20], including 1,405 patients. The characteristics of the seven included trials are summarized in Table I. The PRISMA flowchart of the study selection is shown in Figure 3.

Primary Outcomes: Mortality

We concluded that driving pressure guided ventilation strategy group was significantly associated with decreased mortality among mechanically ventilated patients (RR, 0.56; 95% CI, 0.39-0.79; I^2 = 23%, p<0.05) as shown in Figure

Table I. Characteristics of each study.

Study	Year	Study design	Country	Sample size	Intervention Group size	Primary outcome	Recommendation
Ye et al[15]	2018	RCT	China	60	30	Mortality at day 28	DP guided ventilation strategy is better than PLV titration setting PEEP.
Jiang et al[16]	2021	RCT	China	106	53	postoperative oxygenation index	DP-guided ventilation is associated with a higher OI and less lung injury
Hamama et al[17]	2021	RCT	Egypt	110	55	Mortality at day 28	DP-guided ventilation showed improved survival, Cstat and oxygenation and lower incidence of organ dysfunction for ARDS patients.
Chiumello et al[10]	2016	RCT	Italy	150	108	ICU mortality	Airway driving pressure can detect lung overstress with an acceptable accuracy
Guérin et al[18]	2016	RCT	France	787	533	Mortality at day 90	When PLV is applied to ARDS patients, DP was risk factors for mortality.
Park et al[19]	2019	RCT	Korea	292	145	PPC	Application of DP guided ventilation during one-lung ventilation was associated with a lower incidence of PPC.
Pereira et al[20]	2020	RCT	Brazil	31	16	Mortality at day 28 and variation of DP level	targeting driving pressure may improve the safety of ventilation strategies for ARDS patients

Abbreviations: RCT, Randomized controlled trial; PPC, postoperative pulmonary complications; OI, oxygen index; DP, driving pressure; ICU, intensive care unit.

4. The five eligible documents in this study were tested for heterogeneity, $I^2<50\%$, and the Q test $p>0.1$, indicating that the heterogeneity between the selected documents in this study was not statistically significant, fixed effects were chosen for the meta-analysis. It could be seen from the symmetrical funnel plot that there were no publication bias in the literature of this study (Figure 5).

Secondary Outcomes

Four studies were enrolled in the synthesis. Results indicate that driving pressure (DP) guided ventilation strategy group could have a higher oxygen index compared to the control group, which represented the lung protective ventilation strategy group (MD 43.37, 95%CI 12.58-74.15, $I^2=97\%$, $p<0.05$) (Figure 6). Compared to the DP guided ventilation group, the control group had significantly higher driving pressure level, as shown in Figure 7 (MD -3.03, 95%CI -5.72 – -0.34, $I^2=100\%$, $p=0.03$). There was no statistically significant difference in respiratory compliance, platform pressure, duration of mechanical ventilation, complications, and the length of hospital stays between the DP guided group and control group ($p>0.05$), as shown in Figures 8-12, respectively.

Discussion

In recent years, driving pressure guided mechanical ventilation strategies have been applied in critically ill patients, such as acute respiratory distress syndrome, and Bellani et al[21] study has confirmed that low driving pressure ventilation strategies can improve the prognosis of critically ill patients. Although mechanical ventilation has long been widely used to provide respiratory support for patients undergoing anesthesia surgery and patients with respiratory failure caused by other etiologies, the setting and monitoring of various ventilator parameters are still important

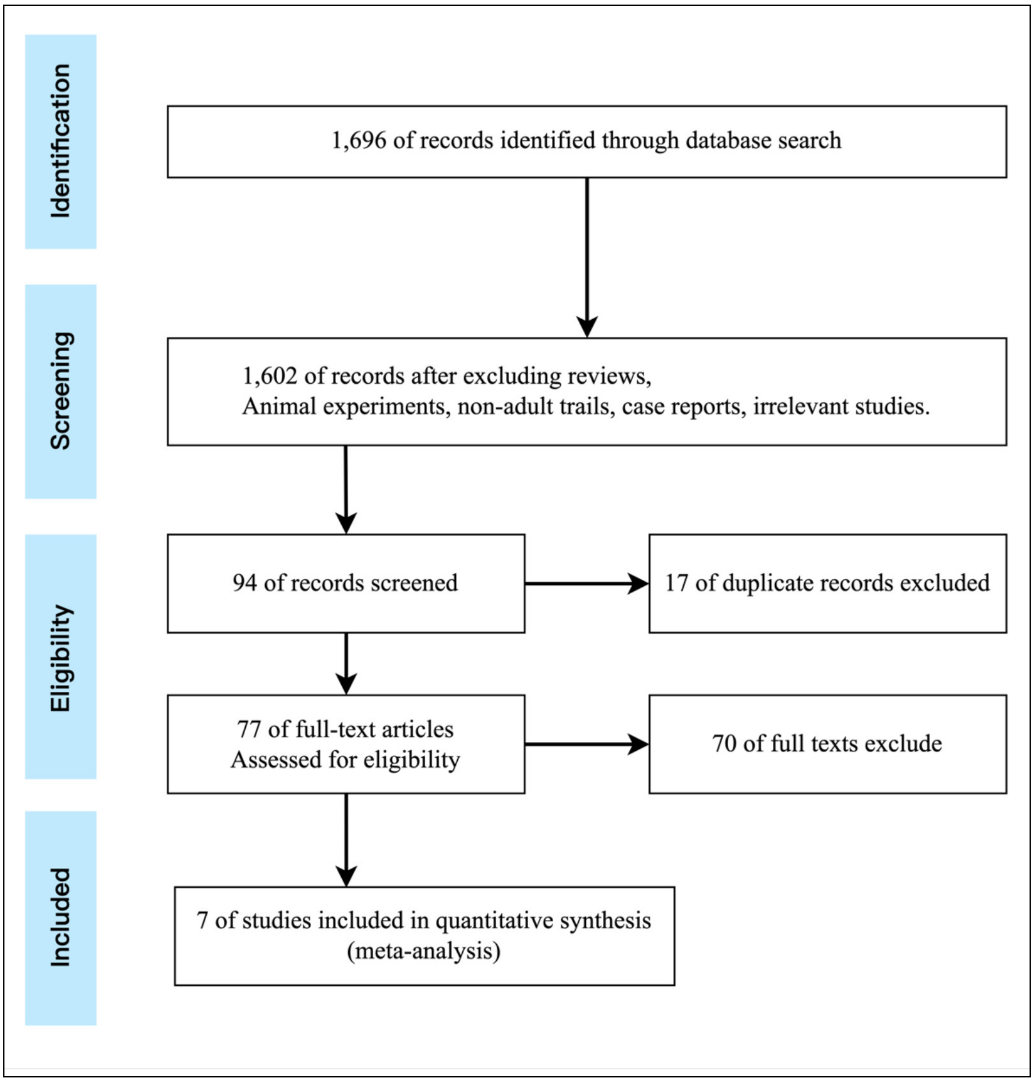

Figure 3. Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) chart identification and selection of studies for inclusion.

in the diagnosis and treatment of various critically ill patients. Such as, the driving pressure has been widely used in clinical practice. A recent meta-analysis[7] investigated the relationship between the driving pressure levels and development of postoperative complications in mechanically ventilated patients under general anesthesia. A study by Del Sorbo et al[22] has shown that the lower driving pressure may provide the better lung-protective ventilation for patients receiving extracorporeal membrane oxygenation (ECMO). This study mainly explores the results and significance of driving pressure in patients receiving mechanical ventilation.

From the meta-analysis of seven studies, we found that the driving pressure-guided ventilation strategy was associated with lower mortality in mechanically ventilated patients compared with the lung protective ventilation group. Amato et al[4] and Bellani et al[21] studies suggested that high driving pressure was associated with increased mortality in patients who received mechanical ventilation. From the perspective of respiratory mechanics, the driving pressure is the ratio of the tidal volume to the compliance of the respiratory system[5]. When the tidal volume is constant, the compliance of the respiratory system is larger and the driving pressure is lower, which indicates that the ventilation at the optimal driving pressure is based on the lung volume of effective ventilation[21]. Both overdistension and insufficient lung air are detrimental; therefore, low driving pres-

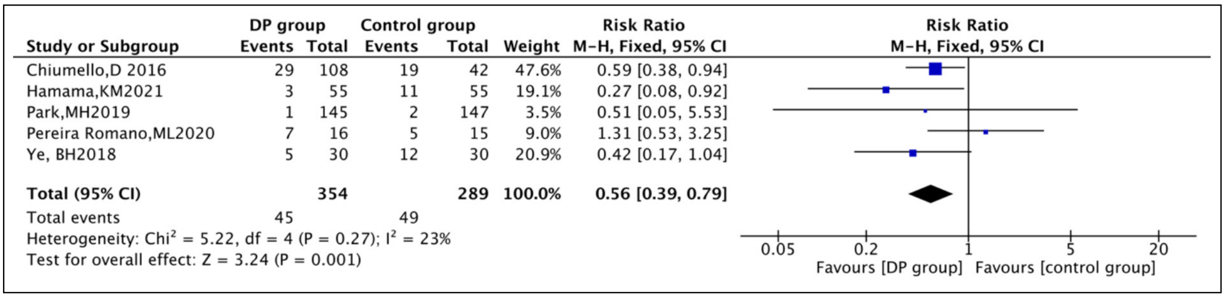

Figure 4. The forest plot of mortality for pooled risk ratio of DP group *vs.* control group which is the lung protective ventilation group from eligible studies.

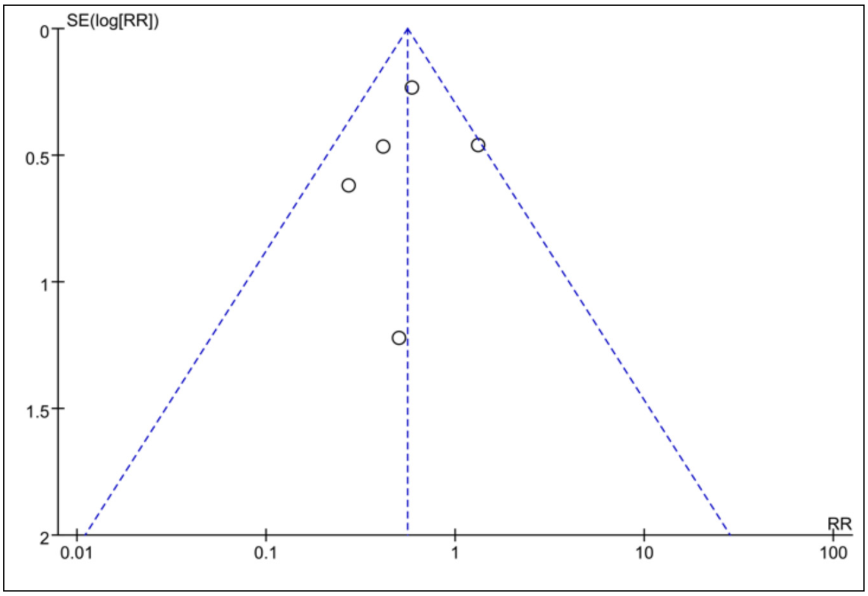

Figure 5. The funnel plot of mortality.

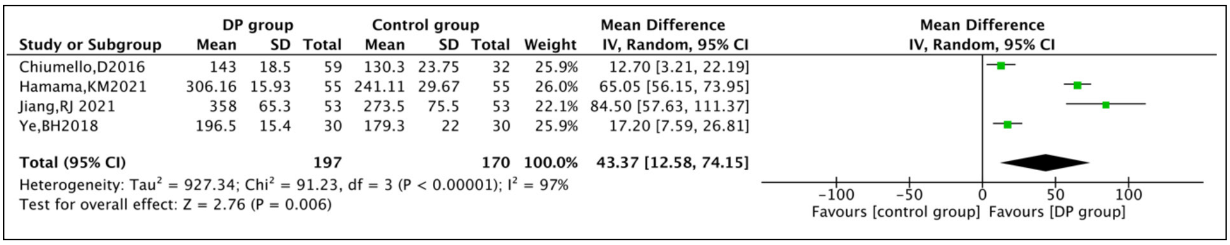

Figure 6. The forest plot of Oxygen Index.

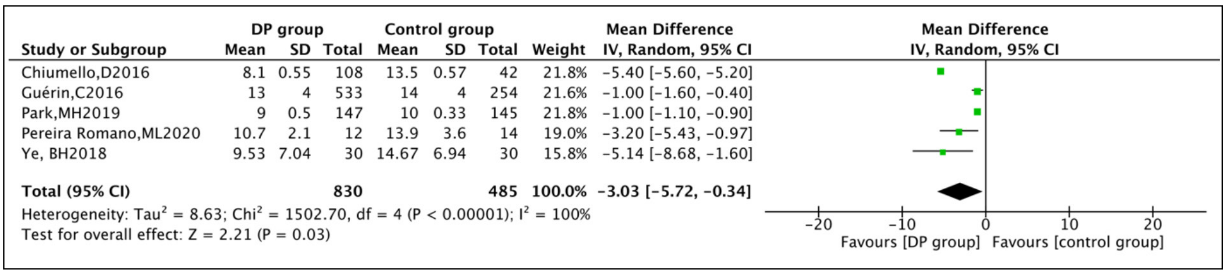

Figure 7. The forest plot of driving pressure.

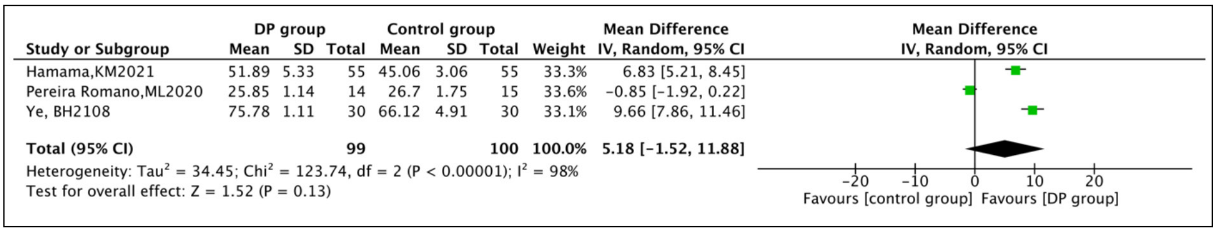

Figure 8. The forest plot of respiratory compliance.

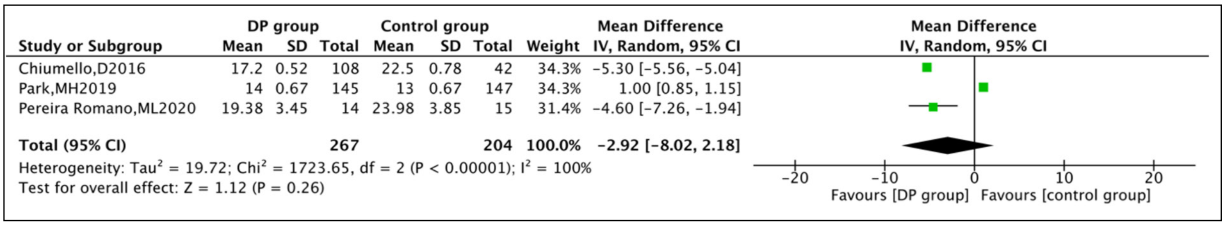

Figure 9. The forest plot of platform pressure.

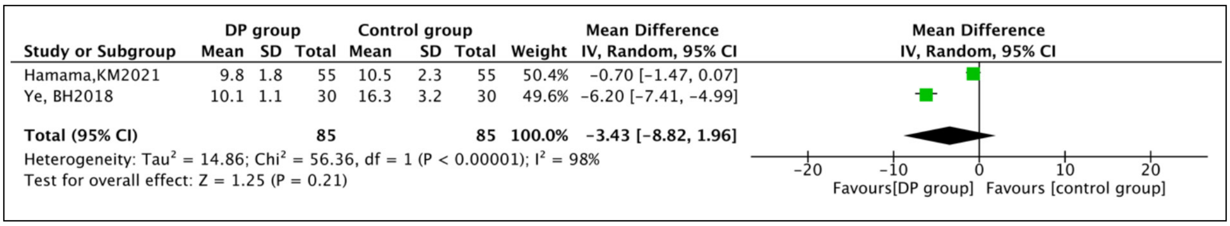

Figure 10. The forest plot of duration of mechanical ventilation.

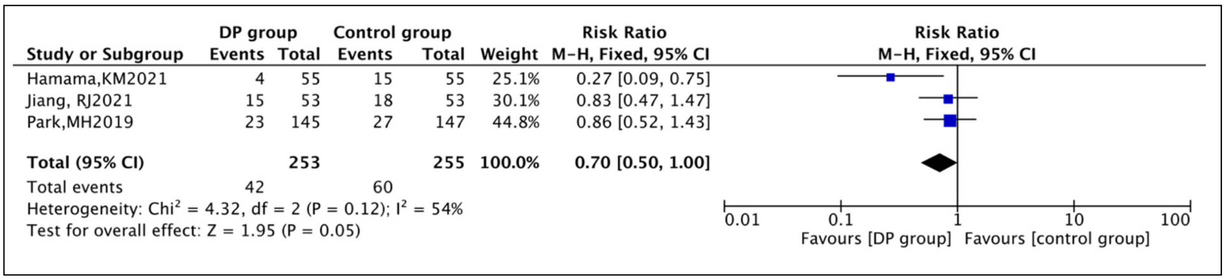

Figure 11. The forest plot of complications.

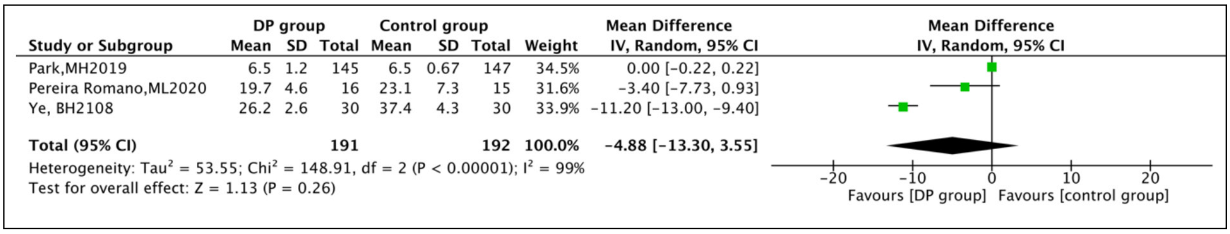

Figure 12. The forest plot of the length of hospital stay.

sure ventilation parameter strategies may reduce lung injury and mortality by reducing volutrauma or atelectasis. Furthermore, driving pressure indirectly reflects lung stress and lung strain through the compliance of the respiratory system. Gattinoni et al[23] research has shown that excessive lung strain and lung stress stimulate macrophages and alveolar epithelial cells to release inflammatory factors and induce lung inflammatory responses, which leads to ventilator induced lung injury

(VILI). Hence, driving pressure guided ventilation group may reduce the lung injury and thus improve the prognosis of patients.

Our study found that DP guided ventilation improved oxygenation. A previous study[15] showed that patients in the low driving pressure group had better lung compliance, so the lower driving pressure the more adequate the alveolar recruitment, which can improve oxygenation. This result is consistent with other research findings, i.e., Mini et al[24] research, which suggested that intraoperative positive end expiratory pressure titration based on minimum driving pressure improves intraoperative oxygenation and postoperative pulmonary function. The driving pressure was lower in the DP guided mechanical ventilation group. The concept of driving pressure guided ventilation increasingly has been used in clinical practice. Some research indicated that a reduction in driving pressure was observed after adjustment of the target tidal volume in the DP limited strategy group[20].

Limitations

Several limitations of this meta-analysis should be discussed. First, not all these trials reported all respiratory related parameters, such as oxygenation index, respiratory compliance and driving pressure etc. Furthermore, findings may be influenced by the diversity of population studied and the variety of diseases receiving mechanical ventilation. Third, one of the studies had a relatively large number of study subjects, which might have influenced the result about driving pressure; hence, we removed this study and then conducted data analysis, which demonstrated that the literature had no impact on the result.

Conclusions

The ventilation strategy guided by driving pressure can reduce the mortality of mechanically ventilated patients, improve the oxygenation index and decrease the level of driving pressure. However, further high-quality studies are still needed to explore the effects of driving pressure-guided ventilation strategies on respiratory mechanics, hemodynamics and complications.

Conflict of Interest

The authors declared no potential conflicts of interest with respect to the research, authorship, and publication of this article.

Authors' Contributions

The corresponding author had full access to all the data in the study and had final responsibility for the decision to submit for publication. Y. Li was responsible for the collection and analysis of data, interpretation of data, writing of the draft manuscript. Q. Zhang was responsible for the collection and analysis of data, interpretation of data; N. Liu contributed to the analysis and interpretation of data. X.Y. Tan contributed to the data analysis. H. Yue contributed to critical revision of the manuscript for content. All authors approved the submission of the final manuscript.

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Ethics Approval

This article does not contain any studies with human participants or animals performed by any of the author.

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