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Research article

Effects of driving pressure-guided ventilation on postoperative pulmonary complications in patients with COVID-19 undergoing abdominal surgery: A post-hoc propensity score-matched analysis

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A R T I C L E I N F O

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A B S T R A C T

Background: Application of individualized positive end-expiratory pressure (PEEP) based on minimum driving pressure facilitates to prevent from postoperative pulmonary complications (PPCs). Whether lung protective ventilation strategy can reduce the risk of PPCs in COVID-19 patients remains unclear. In this study, we compared the effects of driving pressure-guided ventilation with conventional mechanical ventilation on PPCs in patients with COVID-19.
Methods: Patients infected COVID-19 within 30-day before surgery were retrospectively enrolled consecutively. Patients were divided into two group: driving pressure-guided lung protective ventilation strategy group (LPVS group) and conventional mechanical ventilation group (Control group). Propensity score matching for variables selected was used by logistic regression with the nearest-neighbor method. The outcomes were the incidence of PPCs and hypoxemia in post-anesthesia care unit.
Results: There was no significant difference in the baseline data between both groups ($P > 0.05$). The incidence of PPCs (12.73 % vs 36.36 %, $\chi 2 = 7.068$, $P = 0.008$) and hypoxemia [18.18 % vs 38.18 %, $\chi 2 = 4.492$, $P = 0.034$], and lung ultrasound scores [4.68 ± 1.60 vs 8.39 ± 1.87, $t = 8.383$, $P < 0.001$] in LPVS group were lower than control group. The PEEP, airway pressure and plateau pressure in LPVS group were higher than control group, but driving pressure and tidal volume was lower than control group, the difference was statistically significant ($P < 0.05$).
Conclusion: Individualized PEEP ventilation strategy guided by minimum driving pressure could improve oxygenation and reduce the incidence of PPCs in surgical patients with COVID-19.

1. Introduction

Postoperative pulmonary complications (PPCs) are one of the most common respiratory complications in patients who receiving mechanical ventilation under general anesthesia [1,2]. More than 300 million surgeries were performed in the worldwide each year, and approximately 10 % of these patients suffered from PPCs, which was associated with longer hospital stays, costs and higher mortality [3,4].

With the change in the prevention policy of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) since December 2022,

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lots of people suffered from the virus in China. The lung is susceptible to the SARS-CoV-2, and patients within 12 weeks following infection remained a residual reduced lung function and abnormal pulmonary imaging [5,6]. It was reported an increasing incidence of mortality and pulmonary complications in patients undergoing surgery with perioperative SARS-CoV-2 infection [7]. The lung protective ventilation strategy (LPVS) with low tidal volume and positive end-expiratory pressure (PEEP) had been proved to improve oxygenation and reduce the mortality rate in patients with acute respiratory distress syndrome (ARDS) [8]. Meanwhile, the lung protective ventilation strategy was also recommended for patients with high-risk PPCS undergoing elective general anesthesia [9]. However, whether the lung protective ventilation strategies used in patients recovering from SARS-CoV-2 infection can reduce the risk of PPCs remain unclear. This study aimed to compare the effects of lung protective ventilation strategy (LPVS) with individualized PEEP guided by driving pressure on postoperative lung ultrasound scores and the incidence of PPCs with conventional mechanical ventilation in patients recovering from SARS-CoV-2 infection.

2. Patients and methods

2.1. Study design and population

This study was a retrospectively post-hoc propensity score-matched analysis and approved by the Ethics Committee of The First Affiliated Hospital of Wannan Medical College (Ethical Committee NO.83-2022).

Patients undergoing abdominal surgery under general anesthesia who had SARS-CoV-2 infection confirmed within 30 days before surgery, aged ≥18 years, ASA I-III, were included. Major surgery mainly included colorectal, gastrectomy, liver resection, colorectal and pancreaticduodenectomy et al.). Minor surgery included cholecystectomy, appendicectomy and hernia repair surgery et al. Exclusion criteria: (1) patients with a body mass index (BMI) < 18 kg/m^2 or >30 kg/m^2; (2) patients with chronic pulmonary disease, chest wall deformities or a history of thoracic surgery; (3) patients with cardiac, brain and other major systemic diseases; (4) patients received not abdominal surgery; (5) emergency surgery; (6) patients with moderate or severe SARS-CoV-2 infection [10].

2.2. Baseline variables

Information of patients received surgery between November 2022 and March 2023 were retrieved. The clinical data of patients met inclusion criteria were extracted. The demographic characteristics included age, gender, height, weight, ASA physical status, preoperative level of haemoglobin and white blood cell, time of infected with SARS-CoV-2, the history of smoking, chest computed tomography, intraoperative arterial blood gas measurements, type and duration of surgery. The Assess Respiratory Risk in Surgical Patients in Catalonia (ARISCAT) risk index was used to determine the risk of PPCs in surgery patients. The ARISCAT risk index was scored from following variables including age, oxygen saturation, previous respiratory infection, anemia, emergency surgery, abdominal or thoracic surgery, duration of operation [2,11]. In addition, some clinical information included such as lung ultrasound, parameters of ventilation were prospectively registered.

2.3. Definition of ventilation modes

The patients were divided two groups according to the parameters of mechanical ventilation: driving pressure-guided lung protective ventilation strategy (LPVS) group and conventional ventilation strategy group (control group). In LPVS group: volume-controlled ventilation mode was utilized with a tidal volume of 6 ~ 8 ml/kg of ideal body weight, inspiration-to-expiration ratio of 1:2, the fraction of inspired oxygen (F_IO_2) of 0.8 or higher, and optimal individualized PEEP value. The PEEP was titrated by minimum driving pressure (calculated as plateau pressure-PEEP): the PEEP was an increment of 1 cm H_2O from 2 to 14 cm H_2O and maintained for 10 respiratory cycles. The respiratory rate was set to 12 breaths/min and then adjusted to maintain the $PetCO_2$ between 35 and 45 mmHg. In the control group: the ventilation mode was utilized with the same tidal volume, but with a lower level of PEEP (≤5 cmH_2O). The other ventilation parameters were consistent with those in the LPVS group.

2.4. Outcomes

The primary outcome was the incidence of PPCs within 5 days after surgery including severe hypoxemia (SpO_2<90 %), respiratory failure, pleural effusion, atelectasis identified with chest radiography or CT, dyspnea, pneumothorax and ARDS et al. Meanwhile, PPCs was also adjudicated through Melbourne Group Scale Version 2 [11]. The secondary outcomes were the incidence of hypoxemia (SpO_2<90 % in post-anesthesia care unit), postoperative lung ultrasound score, cardiovascular and cerebrovascular events, cardiac arrest and death.

2.5. Statistical analysis

To adjust for potential confounding resulting from significant differences in baseline variables, propensity score matching was used to select the patients in the control group. The propensity score of each patient in the LPVS treatment group was calculated using the gender, age, height, body weight, BMI, ASA physical status, preoperative hemoglobin level, time of infected with SARS-CoV-2, ARISCAT score, history of smoking, and duration of surgery by software SPSS 26.0. Propensity score matching for variables selected was used logistic regression with the nearest-neighbor method.

Kolmogorov-Smirnov analysis was used to test the distribution of the data. Continuous variables were expressed as mean ± standard deviation ($\overline{x} \pm s$)or median (inter-quartile range) and the difference between groups was analyzed by independent samples *t*-test. The categorical variables were expressed as percentages (%), and the difference between groups was analyzed by $\chi 2$ test or Fisher's exact probability. $P < 0.05$ was considered a statistically significant difference.

3. Results

3.1. Patients baseline characteristics

During the study period, a total of 9962 patients' data undergoing surgery under anesthesia were searched. Fifty-five patients met inclusion criteria and were included in LPVS group. After matching against the LPVS group using propensity score matching, 55 of 274 eligible patients with conventional ventilation strategy were included in the control group. A total of 110 patients were finally analyzed. Fig. 1.

There were no statistically significant differences in patients' characteristic such as age, gender, height, weight, BMI, ASA physical status, ARISCAT score, days of infected with SARS-CoV-2, surgical procedure, duration of surgery and preopreative examination ($P >$ 0.05). Table 1.

3.2. Comparison of intraoperative respiratory parameters

The differences in intraoperative arterial blood gas measurements and $PetCO_2$ between the both groups were not statistically significant ($P > 0.05$). The PEEP value (8.52 ± 1.23 vs 3.71 ± 0.82), airway pressure (24.76 ± 3.53 vs 21.68 ± 2.76) and plateau

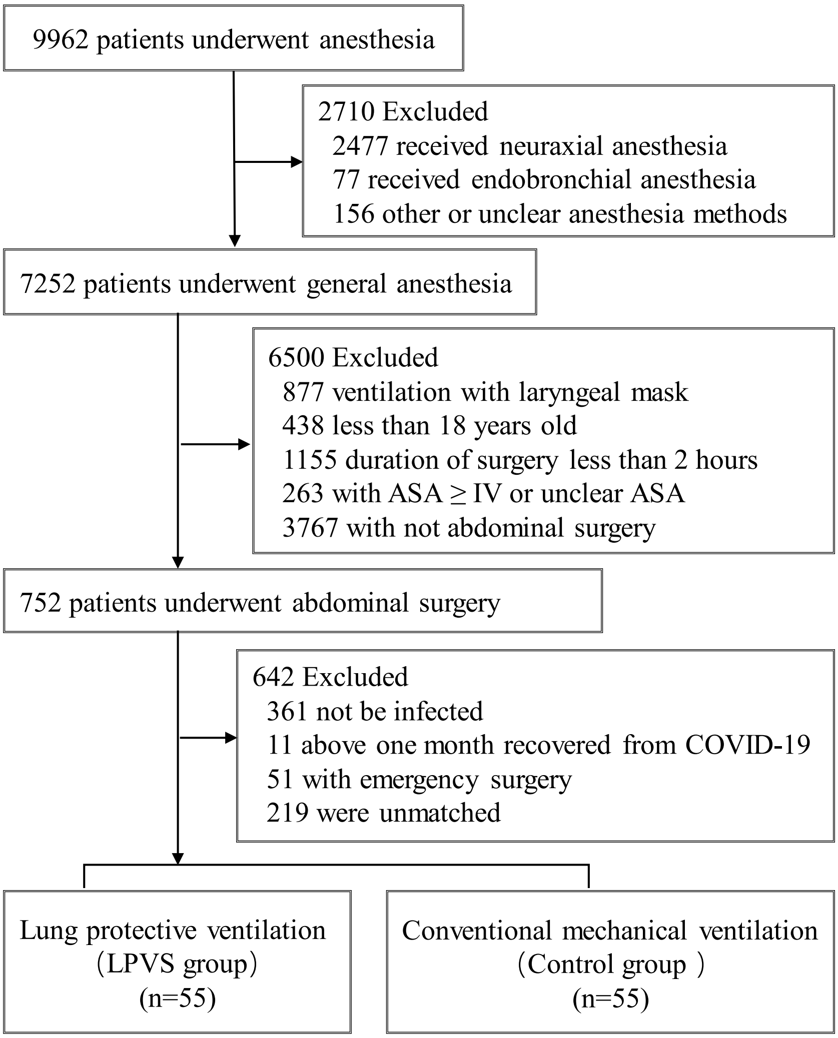

Fig. 1. Flow of patients receiving driving pressure-guided ventilation versus conventional mechanical ventilation.

Table 1
Baseline characteristics [n (%), $\bar{x} \pm s$].

	LPVS group(n = 55)	Control group(n = 55)	$t/\chi 2$ value	P value
Gender			0.156	0.693
Male	22(40.00)	19(34.55)		
Female	33(60.00)	36(65.45)		
Age, y	57.24 ± 10.82	56.95 ± 11.11	0.139	0.890
Height, cm	163.14 ± 5.86	161.33 ± 6.12	1.584	0.116
Weight, kg	58.77 ± 9.39	60.16 ± 7.34	0.865	0.389
BMI, Kg/m^2	22.58 ± 2.87	23.13 ± 2.32	1.105	0.272
ASA physical status			1.046	0.593
I	6(10.91)	4(7.27)		
II	31(56.36)	36(65.45)		
III	18(32.73)	15(27.27)		
Preoperative haemoglobin, g/L	123.12 ± 16.34	118.57 ± 13.59	1.588	0.115
Preoperative white blood cell, $x10^9/L$	7.43 ± 3.12	7.63 ± 2.93	0.780	0.437
Preoperative SpO_2, %	96.75 ± 1.48	97.22 ± 1.32	1.758	0.082
Days with SARS-CoV-2 infection	22.45 ± 4.76	21.03 ± 5.72	1.415	0.160
ARISCAT score	36.82 ± 10.83	35.53 ± 11.77	0.598	0.551
Smoking history			1.420	0.233
Yes	14(25.45)	8(14.55)		
No	41(74.55)	47(85.45)		
Duration of surgery, h	3.31 ± 1.02	3.23 ± 0.98	0.419	0.676
Surgical procedure			0.611	0.434
Major surgery	36 (65.45)	31 (56.36)		
Minor surgery	19 (34.55)	24 (43.64)		
Chest CT			0.073	0.787
Abnormity	7 (12.73)	9 (16.36)		
Non-abnormity	48 (87.27)	46 (83.64)		

Abbreviations: LPVS, lung protective ventilation strategy; BMI, body mass index; ASA, American society of anesthesiologists; ARISCAT, Assess respiratory risk in surgical patients in catalonia; CT, Computed tomography.

pressure (16.43 ± 3.24 vs 13.75 ± 1.78) in LPVS group were statistically higher than those in control group ($P < 0.05$). Compared with control group, the driving pressure (8.54 ± 3.41 vs 10.39 ± 2.47) and tidal volume (389.81 ± 45.71 vs 415 ± 50.12) were statistically lower in the LPVS group ($P < 0.05$). Table 2.

3.3. Postoperative complications

The lung ultrasound score of patients in the LPVS group was 4.68 ± 1.60, which was lower than that of the control group of 8.39 ± 1.87, with a statistically significant difference ($t = 8.383$, $P < 0.001$). There were seven patients (12.73 %) with PPCs and 10 patients (18.18 %) with hypoxemia in the LPVS group and 20 patients (36.36 %) with PPCs and 21 patients (38.18 %) with hypoxemia in the control group. The incidence of PPCs and hypoxemia in the LPVS group were lower than the control group, with a statistically

Table 2
Comparison of intraoperative respiratory parameters and outcomes [n (%), $\bar{x} \pm s$].

	LPVS group (n = 55)	Control group (n = 55)	$t/\chi 2$ value	P value
Tidal volume, ml	389.81 ± 45.71	415 ± 50.12	2.754	0.007
PEEP, cmH_2O	8.52 ± 1.23	3.71 ± 0.82	24.13	< 0.001
Airway pressure, cmH_2O	24.76 ± 3.53	21.68 ± 2.76	5.098	< 0.001
Driving pressure, cmH_2O	8.54 ± 3.41	10.39 ± 2.47	3.258	0.002
Plateau airway pressure, cmH_2O	16.43 ± 3.24	13.75 ± 1.78	5.376	< 0.001
$PetCO_2$, mmHg	40.18 ± 3.82	39.43 ± 4.67	0.922	0.359
Arterial blood gas measurements				
pH	7.34 ± 0.04	7.36 ± 0.07	1.840	0.068
SaO_2, %	97.43 ± 1.69	98.12 ± 2.03	1.937	0.055
PO_2/ FIO_2	406.15 ± 109.27	421.27 ± 111.23	0.719	0.474
$PaCO_2$, mmHg	43.23 ± 5.88	42.84 ± 6.27	0.337	0.737
HCO_3^-, mmol/L	22.69 ± 3.31	23.71 ± 2.87	1.727	0.087
Lactate, mmol/L	1.09 ± 0.62	1.21 ± 0.73	0.929	0.355
Hematocrit, %	33.65 ± 4.18	32.74 ± 3.99	1.168	0.245
Hemoglobin, g/L	111.25 ± 13.34	108.77 ± 12.67	0.999	0.320
Hypoxemia	10(18.18)	21(38.18)	4.492	0.034
PPCs	7(12.73)	20(36.36)	7.068	0.008
Lung ultrasound score	4.68 ± 1.60	8.39 ± 1.87	8.383	<0.001

Abbreviations: LPVS, lung protective ventilation strategy; PEEP, positive end-expiratory pressure; $PetCO_2$, end-tidal CO_2; PPCs; postoperative pulmonary complications.

significant difference ($\chi^2 = 7.068$, $P = 0.008$; $\chi^2 = 4.492$, $P = 0.034$). Based on the sample size and incidence of PPCs in both groups, the power value was 86.33 % with an α of 0.05, indicating a higher statistical power.

There were no patients with cardiovascular and cerebrovascular events, cardiac arrest or death in both groups. Table 2.

4. Discussion

Patients suffered from SARS-CoV-2 may had some symptoms including fever, sore throat, fatigue, cough, dyspnea and even ARDS. These typical manifestations would last up to 6 weeks after recovery [12]. Patients who have recovered from COVID-19 are fragile and more susceptible to postoperative pulmonary complications, and the incidence of PPCs was reported as high as 51.2 % [7,13]. We compared the effects of lung protective ventilation strategy in which individualized PEEP guided by driving pressure on incidence of PPCs with conventional ventilation in patients recovered from SARS-CoV-2 infection and found that the LPVS strategy decreased the risk of hypoxemia and PPCs.

Since the ARMA trial demonstrated that the protective ventilation strategy with a tidal volume of 6 ml/kg and a plateau pressure of less than 30 cmH_2O reduced mortality in patients with ARDS compared with conventional ventilation strategy in 2000, lung protective ventilation strategies have been intensively studied and were recommended as guidelines for the respiratory management of adults with ARDS [14,15]. The concept has now been widely extended to intraoperative respiratory management, but the optimal ventilation parameter settings under general anesthesia remain unclear. Although some studies have investigated this problem, the results are still inconsistent [16–19]. It's may not necessary to conduct the protective ventilation strategy for all surgical patients. For example, for patients with normal lung function, a lower risk of postoperative PPCs, or without undergoing upper abdominal or thoracic surgery, conventional mechanical ventilation did not cause lung injury and not reduced the incidence of PPCs [9]. Therefore, the protective ventilation strategy should be considered using in patients with fragile lung. Impairment of lung tissue is a significant problem in patients with SARS-CoV-2 infection and the pathological mechanism included Diffuse alveolar epithelial injury, hyaline membrane formation, pulmonary capillary injury, alveolar septal fibrosis, and lung consolidation [5,20]. Patients recovered from COVID-19 included in our study were with a high risk of postoperative pulmonary complications and the ARISCAT score was 36.18 ± 11.64. Patients receiving surgery within 6 weeks recovered from SARS-CoV-2 infection is associated with an increased risk of PPCs [21], thus there is greater clinical value in exploring the effectiveness of lung protection strategies in this population.

There is a different pathophysiological behaviour in COVID-19-related ARDS compared with "classical" ARDS and lack of evidence for lung protective ventilation strategy in COVID-19-related ARDS. A cohort study of 1503 critically ill patients with COVID-19 infection found that lung protective ventilation strategy conducting within 24 h admission to ICU reduced 28-day mortality [22]. The latest guidelines recommended the lung protective ventilation strategy (tidal volume 6 ml/kg, plateau pressure <30 cmH_2O, driving pressure <15 cmH_2O) could achieve a better clinical outcome in patients with COVID-19 [23,24]. Recently, the protective effect of low tidal volumes is widely accepted, but the advantages of high or low PEEP and individualized PEEP have been debated. In other words, higher PEEP level is not always superior to low PEEP level in lung protective ventilation, and LPVS strategy with higher PEEP levels have not been found to reduce the incidence of PPCs in open abdominal surgery [20]. Additionally, patients with COVID-19-related ARDS usually required higher levels of PEEP than "classic" ARDS under oxygenation conditions, suggesting that this population is more susceptible to barotrauma. Anesthesiologists should pay more attention to individualized PEEP when performing intraoperative lung protective ventilation strategy [25].

Airway driving pressure is the direct driver of the expansion of the entire respiratory system, a more precise way of normalizing tidal volumes to size of lung from a physiological point of view, also represented as the difference between plateau pressure and PEEP from a respiratory mechanics perspective, comprehensively reflects respiratory system mechanics and ventilation settings [26]. Adjusting tidal volume and PEEP can achieve the minimum driving pressure, at the time pulmonary compliance is of greatest. More recently, studies have demonstrated driving pressure-guided individualized PEEP ventilation strategy can improve pulmonary compliance and oxygenation, and facilitates to prevent PPCs compared with fixed PEEP of 5 cmH_2O [27,28]. Our study also indicated that individualized PEEP guided by minimum driving pressure reduced the incidence of PPCs in patients infected with COVID-19. In addition, the optimal PEEP value 8.52 ± 1.23 cmH_2O in present study, which was a desired moderate PEEP (7–9 cmH_2O). The result was consistent with previous studies [29].

Of course, there are certain limitations in our study. (1) The PEEP in control group was limited less than 5 cmH_2O, PEEP was not used in some patients during mechanical ventilation. Therefore, whether individualized PEEP guided by driving pressure is superior to a fixed PEEP needs further research. (2) Different from previous study in which a decremental PEEP titration protocol was used [30], an incremental protocol was applied in this study. At the beginning of the experiment, PEEP is likely to be lower than alveolar pressure. This may cause collapse of some alveoli again, offsetting the effect of recruitment. However, considering that patients infected with COVID-19 have a high airway pressure and was more susceptible to barotrauma, the incremental protocol was safer. Nevertheless, it is not clear whether decremental and incremental protocols are equivalent in setting the optimal PEEP. (3) Considering ethics and safety, patients with moderate or severe infection and those who still have significant symptoms were excluded, whether the results are available for this population is unclear. (3) Previous study reported that the incidence of PPCs in postoperative patients was 51.2 % [7], but the incidence of PPCs in this trial was lower than that. This is related with the implementation of lung protective ventilation strategy, SARS-CoV-2 different variants, inclusion of only mild patients and smaller sample.

5. Conclusions

The COVID-19 pandemic seems to have come to an end, but the impacts of COVID-19 sequelae on people's health may continue.

Now many people are suffering from the reinfection of COVID-19 and more and more patients would suffer from surgery following COVID-19 infection in future, which bring new challenges to perioperative management, especially for respiratory management. This study found that individualized PEEP guided by driving pressure can improve oxygenation, reduce the risk of postoperative pulmonary complications and be worthy of clinical application.

Ethics statement

The study was approved by the Ethics Committee of The First Affiliated Hospital of Wannan Medical College (Ethical Committee NO.83-2022). The data has been completely anonymised to remove any identifying patient's information. The study complied with the Reporting of Observational Studies in Epidemiology guidelines.

Data availability statement

Individual participant data will not be made available. The data analyzed during the current study will be available on request.

CRediT authorship contribution statement

Na Wei: Writing – review & editing, Formal analysis. **Jun-Sheng Chen:** Writing – original draft, Data curation. **Bang-Sheng Hu:** Formal analysis, Data curation. **Ya Cao:** Supervision, Methodology. **Ze-Ping Dai:** Supervision, Project administration, Funding acquisition.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.heliyon.2024.e25533.

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