Effect of ventilation strategy during cardiopulmonary bypass on postoperative pulmonary complications after cardiac surgery: a randomized clinical trial

Meng-Qiu Zhang¹, Yu-Qi Liao², Hong Yu¹, Xue-Fei Li¹, Wei Shi¹, Wei-Wei Jing¹, Zai-Li Wang¹, Yi Xu¹ and Hai Yu¹*

Abstract
Background: To determine whether maintaining ventilation during cardiopulmonary bypass (CPB) with a different fraction of inspired oxygen (FiO₂) had an impact on the occurrence of postoperative pulmonary complications (PPCs).

Methods: A total of 413 adult patients undergoing elective cardiac surgery with CPB were randomly assigned into three groups: 138 in the NoV group (received no mechanical ventilation during CPB), 138 in the LOV group (received a tidal volume (VT) of 3–4 ml/kg of ideal body weight with the respiratory rate of 10–12 bpm, and the positive end-expiratory pressure of 5–8 cmH₂O during CPB; the FiO₂ was 30%), and 137 in the HOV group (received the same ventilation parameters settings as the LOV group while the FiO₂ was 80%).

Results: The primary outcomes were the incidence and severity of PPCs during hospitalization. The composite incidence of PPCs did not significantly differ between the NoV (63%), LOV (49%) and HOV (57%) groups (P = 0.069). And there was also no difference regarding the incidence of PPCs between the non-ventilation (NoV) and ventilation (the combination of LOV and HOV) groups. The LOV group was observed a lower proportion of moderate and severe pulmonary complications (grade ≥ 3) than the NoV group (23.1% vs. 44.2%, P = 0.001).

Conclusion: Maintaining ventilation during CPB did not reduce the incidence of PPCs in patients undergoing cardiac surgery.

Trial registration: Chinese Clinical Trial Registry ChiCTR1800015261. Prospectively registered 19 March 2018. http://www.chictr.org.cn/showproj.aspx?proj=25982

Keywords: Cardiac surgery, Cardiopulmonary bypass, Mechanical ventilation, Fraction of inspired oxygen, Postoperative pulmonary complications

Background
Every year, over 1.25 million patients undergo cardiac surgery utilizing cardiopulmonary bypass (CPB) globally, with approximately 180,000 of those operations conducted in China [1]. Postoperative pulmonary complications (PPCs), including pneumonia, pleural effusion, atelectasis, etc., are common, with reported incidence of up to 59.2% [2]. These well-documented complications...
prolong the hospital stay and increase in-hospital mortality after surgery [3].

Attempts concentrating on lung-protective ventilation strategies have been made to prevent PPCs. The intraoperative lung-protective ventilation bundle has been identified as an independent association with reduced PPCs after cardiac surgery [4]. Mechanical ventilation with low tidal volume ($V_T$) during CPB appears to be beneficial [5], though conflicting data exist [6, 7]. A recent meta-analysis indicated that the ventilation during CPB may improve the gas exchange and oxygenation index (OI), while the long-term outcomes are unknown. And the settings of the fraction of inspired oxygen ($FiO_2$) may make a difference [8]. Moreover, recently published guidelines on CPB in adult cardiac surgery recommend that "PEEP during CPB should be considered in order to protect the lungs" and "Ventilation during CPB may be considered for lung protection" (level of evidence B) [9]. In addition, the arguments both for and against the use of hyperoxia for lung protection are still ongoing [10, 11]. However, the effect of low $V_T$ ventilation with different $FiO_2$ during CPB in patients having cardiac surgery is still unclear.

Therefore, we conducted this pragmatic randomized trial to investigate the effect of ventilation with different $FiO_2$ or suspended ventilation during CPB on the occurrence of PPCs in patients undergoing cardiac surgery.

Methods

Trial design and overview

This prospective randomized, controlled, patient-and-evaluator-blinded trial was implemented over the period from May 2018 to March 2019. It was approved by the Ethics Committee of West China Hospital of Sichuan University and registered before participant enrolment at the Chinese Clinical Trial Registry (ChiCTR1800015261). Written informed consent was obtained from each participant in the ward before the day of surgery. The study protocol has been published elsewhere [12]. This study combined different ventilation strategies and different $FiO_2$. Briefly, the patients were randomized into three groups: (1) the NoV group: no ventilation during CPB; (2) the LOV group: participants received a low $V_T$ of 3–4 ml/kg of ideal body weight (IBW) with the respiratory rate (RR) of 10–12 bpm, and the positive end-expiratory pressure (PEEP) of 5–8 cmH2O during CPB; the $FiO_2$ is 30% with a flow of 2 L/min; (3) the HOV group: the $FiO_2$ is 80% with a flow of 2 L/min; the ventilation parameter settings were same as the LOV group.

Study population

Patients undergoing elective cardiac surgery (age ≥ 18 years old) with CPB were recruited in the trial. Patients having pregnant and those who have long-term use of hormone therapy before surgery (≥ 3 months) or have already participated in other similar researches within 3 months were excluded from the participation. Heart transplantation, pulmonary thromboendarterectomy, aortic arch, and other deep hypothermic circulatory arrest surgeries and concomitant other non-cardiac interventions were also excluded.

Randomization and blinding

According to the randomization list generated by Microsoft Excel, all patients were allocated in a 1:1:1 treatment ratio to one of the three groups: (1) the NoV group; (2) the LOV group; (3) the HOV group. One investigator not involved in the trial was responsible for screening and grouping the patients. He reviewed the patients’ hospitalized records on the day before surgery, interviewed patients who met the criteria, and signed informed consent. He would also pass the opaque, sealed, and sequentially numbered envelopes to the attending anesthesiologists, who were in charge of patients’ treatments. The attending anesthesiologists and surgeons were not blinded due to the characteristics of the study. The patients, the data collectors, evaluators and the intensivists, respiratory therapists (RTs) were unaware of the allocation and intervention information.

Anesthesia and perioperative care

No pre-medication was administered. Intraoperative monitoring included five-lead electrocardiogram, invasive artery blood, central venous pressure, pulse oxygen saturation, end-tidal carbon dioxide partial pressure ($P_{ET}CO_2$), transesophageal echocardiogram, nasopharyngeal temperature, and bispectral index (BIS).

Induction medication was decided by the attending anesthesiologists. Preoxygenation for denitrogenation was administrated before endotracheal intubation. Continuous infusing remifentanil, combined with sevoflurane and/or propofol to maintain the BIS level between 40 and 60. After intubation, volume-controlled ventilation strategy was applied with the following settings: $V_T=6–8$ ml/kg IBW, PEEP = 5–8 cmH2O, I/E ratio = 1:2, $FiO_2 = 50\%$, and RR = 10–12 bpm, maintaining $P_{ET}CO_2$ between 35 and 45 mmHg, intermittent vital capacity maneuvers (VCMs) were carried out with manual ventilation creating the airway pressure at 30 cmH2O for at least 5 s at the end of CPB and before transferring out of the operation room. Heparin 3 mg/kg was given intravenously to obtain an activated clotting time (ACT) of 480 s to start the CPB. PaO2 during CPB was maintained between 150 and 250 mmHg and mean arterial blood pressure was maintained between 50 and 70 mmHg. At the end of CPB, heparin was antagonized by protamine in a dose of 1:1 to bring ACT to baseline levels.
Synchronized intermittent mandatory ventilation was applied immediately after patients were transferred to the ICU. The ventilation parameter settings were as follow: \( V_T = 6-8 \) ml/kg IBW, PEEP = 8 cmH\(_2\)O, RR = 12 bpm, \( \text{FiO}_2 = 50\% \). \( \text{FiO}_2 \) was adjusted according to the PaO\(_2\) by performing arterial blood gas analyses. \( \text{FiO}_2 \) was decreased by 10\% if lower than 80 mmHg, increased by 10\% if lower than 80 mmHg. The minimum \( \text{FiO}_2 \) was 30\%. Other therapeutic approaches and decisions were all up to the ICU physicians.

**Data collection**

Data were independently collected by a researcher who was blinded to treatment assignment and also not involved in the clinical care decision making. Baseline characteristics included gender, age, body mass index, smoking history, pulmonary diseases, hypertension, and diabetes mellitus. Intraoperative data included types and duration of surgery, duration of CPB, and aortic cross-clamp (ACC), allogeneic red blood cell unit. Postoperative data included the intubation time and the length of ICU and hospital stay.

**Outcomes**

The primary outcomes were the composite incidence of the PPCs [13] (Additional file 1: Table S1) and the PPCs severity score [14] (Additional file 1: Table S2) during the hospital stay. Chest radiographs were obtained for all patients in the first 24 h after surgery in addition to those requested by the ICU physician. The occurrence and severity of PPCs were assessed daily, until hospital discharge, using the worst score during the hospital stay for the main analyses. Each postoperative pulmonary complication, the worst patients experienced throughout their hospital stay, was graded from 1 to 5. The higher the grade was, the worse the condition. Pulmonary complications were defined according to symptom, sign, and chest imaging examination. Patients with symptoms of pulmonary complications were examined by chest radiographs or CT according to clinical practice by the attending physician. All chest imaging was evaluated by the blinded attending radiologist. Arterial blood gas analyses would be administrated when shortness of breath, dyspnea, or \( \text{SpO}_2 < 92\% \) occurs. The complications were measured by outcome evaluators and surgeons together. The second outcomes were OI (calculate as: \( \text{OI} = \frac{\text{PaO}_2}{\text{FiO}_2} \)), surgical site infection, intubation time, length of ICU stay, hospital stay, and in-hospital and 30-d mortality. The occurrence of OI<300 mmHg was compared at three time points: the moment arriving in the ICU, 6, and 12 h after arrival in the ICU.

**Statistical methods**

Due to the limited data on the effect of ventilation strategies during CPB on PPCs when the study was designed, we conducted a pilot study to preliminarily observe the incidence of PPCs in our center. The sample size was determined to obtain 80\% power to show an 18-point absolute difference in the occurrence of PPCs during hospital stay between the two groups (40\% in the NoV group vs. 22.2\% in the LOV group, based on the pilot study). We calculated that 127 patients per group were needed with a 2-sided \( \alpha = 0.05 \). To allow for 10\% attrition, 420 patients were needed (140 patients per group).

Outcomes data were analyzed in the intention-to-treat (ITT) population. The Kolmogorov–Smirnov and Levene’s test were used to analyse the normality and variance homogeneity. The normally distributed continuous data satisfying the homogeneity of variance were presented as mean [standard deviation (SD)] and compared using one-way analysis of variance (ANOVA). Fisher’s least significant difference-t test (LSD-t test) was used for post hoc analysis. The non-normally distributed and ordinal data were presented as median (inter-quartile range) and compared using the non-parametric Kruskal–Wallis test. When significant differences were found, the test was followed by pairwise comparison using the Mann-Whitney U-test, with Bonferroni adjustment for multiple tests (three comparisons). The categorical data were presented as the number (percentage) and compared using the Pearson \( \chi^2 \) test or Fisher’s exact test. Statistical analyses were accomplished with SPSS 20.0 (IBM, Chicago, IL, USA).

To maintain an overall familywise error rate of less than 0.05, the threshold for type I error rate was adjusted for each of the two co-primary outcomes to 0.025 (2-sided). Furthermore, a Bonferroni-adjusted \( P \)-value < 0.0083 (0.025/3) was considered statistically significant to control type I error for the pairwise comparisons between the three groups [15].

**Results**

**Study population**

Enrolment ceased when the target sample size was obtained. A total of 420 patients were randomized in the study and 140 patients were randomized into each group initially. Seven patients were excluded because of the cancellation of surgery. Therefore, 413 patients completed the study and were included in the data analyses (Fig. 1). There were no significant differences in baseline characteristics and intraoperative variables among the three groups (Table 1).
Primary outcomes
Patients who experienced at least one episode of respiratory failures, respiratory infection, pleural effusion, atelectasis, aspiration pneumonitis, bronchospasm, or pneumothorax or any combination of these during hospital stay were considered to have PPCs. The composite incidence of PPCs was 63% in the NoV group, 49% in the LOV group, and 57% in the HOV group ($P=0.069$; Table 2). Also, no difference was observed for this outcome in the combined ventilation groups compared with that in the no ventilation group (53% versus 63%; odds ratio [OR], 0.66; 95% confidence interval [CI], 0.44–1.01; $P=0.054$). There was also no statistical difference among the three groups in the comparison of each complication event (Table 2). The incidence of moderate and severe pulmonary complications (grade $\geq 3$) that occurred in LOV group was significantly lower than that in NoV group ($P=0.001$) (Fig. 2).

Other outcomes
In the comparison of OI among the three groups in the time points of 6 h and 12 h after arrived ICU. The LOV group was superior to the NoV group in those two time points ($P=0.003$ and 0.016, respectively) (Fig. 3). There was no significant difference in surgical site infection, ICU intubation time, ICU stay, hospital stay, and in-hospital and 30-d mortality among the three groups (Table 2).

Discussion
This study revealed that continuation of low $V_T$ ventilation with 30% or 80% FiO$_2$ were not superior to no ventilation during CPB, with respect to the incidence of PPCs during hospital stay after surgery. However, given the study design, it was also difficult to draw strong conclusions on the application of low $V_T$ ventilation with 30% FiO$_2$ may reduce the severity of PPCs. The lungs are particularly vulnerable during cardiac surgery. Adequate intraoperative pulmonary management and monitoring are paramount in preventing post-cardiac pulmonary complications. However, the traditional practice is to suspend ventilation during CPB for the best exposure of the surgical field [16]. The goal of this trial was to investigate whether the use of low $V_T$ ventilation with different level of FiO$_2$ or not during CPB has an influence on PPCs. The composite incidence of PPCs in this study is relatively high, which only reflects the situation of our single medical center. Maintaining low $V_T$ ventilation combined with different FiO$_2$ during
| Table 1  | Baseline characteristics and surgical data |
|----------|------------------------------------------|
|          | NoV (n = 138)                           | LOV (n = 138) | HOV (n = 137) | P value |
| Age (year)                      | 53 (46–61)                              | 52 (45–63)   | 52 (46–61)   | 0.796   |
| Gender (M/F), n                  | 62/76                                   | 64/74        | 67/70        | 0.800   |
| Smoking, n (%)                   | 31 (22.5)                               | 30 (21.7)    | 31 (22.6)    | 0.982   |
| BMI                                 | 23.1 (20.7–25.2)                        | 22.6 (20.7–25.1) | 23.2 (20.9–25.1) | 0.650   |
| ASA III, n (%)                   | 134 (97.1)                              | 137 (99.3)   | 136 (99.3)   | 0.339   |
| EuroScore II                      | 1.07 (0.84–1.39)                       | 1.07 (0.86–1.51) | 1.02 (0.86–1.35) | 0.683   |
| Preoperative OI                   | 385 (376–404)                           | 385 (365–404) | 385 (371–409) | 0.485   |
| Comorbidities, n (%)             |                                        |              |              |         |
| COPD                               | 3 (2.2)                                 | 6 (4.3)      | 5 (3.6)      | 0.629   |
| Hypertension                      | 23 (16.7)                               | 18 (13.0)    | 22 (16.1)    | 0.669   |
| Diabetes                           | 5 (3.6)                                 | 7 (5.1)      | 12 (8.8)     | 0.172   |
| Prior stroke                       | 3 (2.2)                                 | 3 (2.2)      | 5 (3.6)      | 0.693   |
| Surgical type, n (%)             |                                        |              |              |         |
| Valve replacement/repair          | 116 (84.1)                              | 113 (81.9)   | 120 (87.6)   | 0.419   |
| CABG                               | 11 (8.0)                                | 11 (8.0)     | 9 (6.6)      | 0.878   |
| Repair of structural defect       | 16 (11.6)                               | 23 (16.7)    | 17 (12.4)    | 0.418   |
| Resection of a cardiac tumour     | 1 (0.7)                                 | 3 (2.2)      | 3 (2.2)      | 0.643   |
| Anesthetics administration        |                                        |              |              |         |
| Sufentanil (ug/kg)                | 2.7 (2.2–3.5)                           | 3.3 (2.6–4.1) | 2.9 (2.5–3.9) | 0.661   |
| Cisatracurium (mg/kg)             | 0.60 (0.5–0.8)                          | 0.70 (0.5–0.9) | 0.70 (0.4–0.8) | 0.856   |
| Duration of surgery (min)         | 235 (196–291)                           | 240 (203–280) | 245 (210–286) | 0.851   |
| Duration of CPB (min)             | 116 (93–140)                            | 117 (95–155) | 123 (90–154) | 0.737   |
| Duration of ACC (min)             | 77 (65–105)                             | 83 (60–110)  | 83 (60–113)  | 0.661   |
| ACC ≥ 90 min, n (%)               | 62 (44.9)                               | 50 (36.2)    | 60 (43.8)    | 0.281   |
| Application of NIV in ICU, n (%)  | 51 (36.9%)                              | 64 (46.4%)   | 47 (34.3%)   | 0.098   |
| Intraoperative infusion (L)       | 1.2 (1.0–1.4)                           | 1.2 (1.0–1.5) | 1.2 (0.9–1.5) | 0.532   |
| Allogeneic RBC (u)                | 2 (0–6)                                 | 2 (0–8)      | 1 (0–8)      | 0.121   |

BMI: body mass index; ASA: American Society of Anesthesiologists; OI: oxygenation index; COPD: chronic obstructive pulmonary disease; CABG: coronary artery bypass graft; CPB: cardiopulmonary bypass; ACC: aortic crossclamp; NIV: non-invasive ventilator; ICU: intensive care unit; RBC: red blood cells

| Table 2  | Outcomes |
|----------|----------|
|          | NoV (n = 138) | LOV (n = 138) | HOV (n = 137) | P value |
| Primary outcome                      |                |              |              |         |
| Composite incidence, n (%)           | 87 (63)        | 68 (49)      | 78 (57)      | 0.069   |
| Pleural effusion (needing thoracentesis) | 46 (33) | 39 (28)      | 32 (23)      | 0.185   |
| Respiratory failure                  | 21 (15)        | 19 (14)      | 17 (12)      | 0.796   |
| Respiratory infection                | 29 (21)        | 20 (15)      | 25 (18)      | 0.366   |
| Pulmonary atelectasis                | 22 (16)        | 19 (14)      | 32 (23)      | 0.092   |
| Pneumothorax                         | 5 (4)          | 2 (2)        | 3 (2)        | 0.490   |
| Aspiration pneumonia                 | 0              | 0            | 0            | –       |
| Bronchospasm                         | 0              | 0            | 0            | –       |
| Secondary outcomes                  |                |              |              |         |
| Surgical site infection, n (%)       | 4 (2.9)        | 3 (2.2)      | 2 (1.5)      | 0.913   |
| ICU intubation time (h)              | 14.5 (8.4–35.3)| 15.5 (9.0–37.3)| 16.0 (9.0–35.0) | 0.896   |
| Duration of ICU (d)                  | 3 (2–4)        | 3 (2–4)      | 3 (2–4)      | 0.697   |
| Hospital stay (d)                    | 8 (7–10)       | 8 (6–10)     | 8 (6–10)     | 0.837   |
| Hospital mortality, n (%)            | 4 (2.9)        | 3 (2.2)      | 2 (1.5)      | 0.913   |
| 30-d mortality, n (%)                | 5 (3.6)        | 4 (2.9)      | 4 (2.9)      | 0.701   |
CPB did not reduce the incidence of PPCs. The incidence of PPCs in our study is 56%. With similar findings, the incidence of PPCs in the PROVECS trial was also high (59.2%) [2]. That study found that maintaining mechanical ventilation with higher PEEP level during CPB did not reduce PPCs, as compared with a conventional strategy with no ventilation during CPB and lower PEEP level. And all the participants were received a 40% FiO2 during CPB. It is the first prospective study to assess pulmonary complications, which is highly relevant to clinical practice. The incidence of PPCs in that trial is similar to our LOV group’s, probably due to the similarity of design.

The top three incidences of PPCs in our study were pleural effusion, atelectasis, and pulmonary infection, which is consistent with the results of a previous study [17], while that in the PROVECS trial were respiratory failure, respiratory acidosis, and radiological atelectasis [2]. The surgical type in our study is mainly valvular procedure (over 80%) due to rheumatic heart disease, which is much higher than the PROVECS’s. And the subjects in that study were older than our subjects. These may lead to a difference in the incidence of PPCs.

In the present study, the proportion of moderate and severe pulmonary complications in the LOV group was
21% lower than that in the NoV group (23% vs. 44%; OR, 0.38; 95% CI, 0.23–0.64; \( P = 0.001 \)). It indicated that a low \( V_T \) ventilation strategy with 30% \( \text{FiO}_2 \) may attenuate the severity of pulmonary complications. Previous studies have not used this parameter as a primary comparison indicator. Similar to that result, the LOV group had higher OI at 6 and 12 h after arrival in the ICU than the NoV group. This result is consistent with Beer’s study [18], in which the participants received a \( V_T \) of 3–4 ml/kg ventilation during CPB. They found that the ventilated group has higher OI than the unventilated group at the end of the operation and 6 h, 12 h after arrival in the ICU. Even if there was no difference in postoperative ventilator support time between the two groups, they still suggested that maintaining ventilation during CPB was superior in reducing postoperative lung injury. However, the increased OI did not influence the incidence of PPCs or other outcomes, such as intubation time and in-hospital mortality in our study. A lower incidence of moderate to severe PPCs in the LOV group as compared to the NOV and HOV groups as well as better OI primarily at 6 h after surgery, thus implying a biphasic effect of \( \text{FiO}_2 \). Determining whether low \( V_T \) ventilation with different \( \text{FiO}_2 \) during CPB provides clinical benefit in cardiac surgical patients is challenging, because procedure-related pulmonary complications may obscure the benefits from a relatively brief duration of mechanical ventilation during CPB. The efficacy of low \( V_T \) ventilation combined with different \( \text{FiO}_2 \) during CPB shows here, together with the low effort and zero costs necessary for implementation and with no side effects observed or expected, makes it hard to argue against using this simple method for reduction of PPCs.

The most recently published, MECANO trial recruited a large number of patients (\( n = 1501 \)). No differences were observed between the VENT group (5 bpm with a \( V_T \) of 3 ml/kg and PEEP of 5 cmH\(_2\)O) and the control group (no ventilation) in the hospital mortality, early respiratory failure, ventilation support beyond day 2 and reintubation. Unlike our study, more than half of the types of surgery are CABG (62%). Yet, the results were similar to our study, without any difference regarding clinical outcomes between the two groups, such as PPCs and in-hospital mortality [19].

There are also some limitations to this study. First, this was a single-center study, all of the perioperative management were carried out according to our hospital’s clinical practice. Second, in the type of surgery, the majority of patients (> 80%) underwent valvular surgery due to rheumatic heart disease. Therefore, the conclusion drawn by our study should be carefully applied to other medical centers. Third, such a difference between expected and observed incidence of pulmonary complications may have implications in the required sample size and study power. Notably, absolute risk reduction is 14%, and a relative risk reduction of 22% with a no costs intervention are significant findings and should not be diminished by the firm conclusions. The use of composite outcomes also offers the interest to reduce sample sizes; however, it may be responsible for difficulties in the interpretation of the results. Nonetheless, for each component included in our composite outcome, the differences in the degree of severity and the incidence had been compared. Fourth, we only applied the volume-controlled ventilation mode in the study. It is also unclear that which ventilation mode (volume-controlled or pressure-controlled ventilation) is superior, though a previous study suggested there is no difference between them [20]. Fifth, in consideration of maintaining hemodynamic stability, administering VCMs was not standard as reported in the literature [21], but we can ensure the effectiveness of the maneuvers for reopening the collapsed lung. We also didn’t record the detailed usage of inotrope, left ventricular function, and other intraoperative ventilation-related parameters such as peak inspiratory pressure. Whether there is a difference in those patients is unclear. Given that the management of the ICU were carried out by the intensivists and RTs, the effects of our interventions may be obscured by the supplementary oxygen therapies and prolonged ventilation time.

**Conclusion**

In conclusion, our study showed that maintaining low \( V_T \) ventilation combined with different \( \text{FiO}_2 \) during CPB did not reduce the incidence of PPCs in comparison to the conventional strategy with no ventilation. Though a difference was not confirmed and no clinically relevant difference was observed, the application of low \( V_T \) ventilation with 30% \( \text{FiO}_2 \) during CPB may have a trend to attenuate the severity of PPCs.

**Abbreviations**

ACT: Active clotting time; ACC: Aortic cross clamp; ANOVA: Analysis of variance; BIS: Bispectral index; CPB: Cardiopulmonary bypass; \( \text{FiO}_2 \): Fraction of inspired oxygen; IBW: Ideal body weight; ITT: Intention-to-treat; OI: Oxygenation index; PPCs: Postoperative pulmonary complications; \( \text{PaO}_2 \): Partial pressure of arterial oxygen; PEEP: Positive end-expiratory pressure; \( P_{\text{ETCO}_2} \): End-tidal carbon dioxide partial pressure; RCTs: Randomized controlled trials; RR: Respiratory rate; SD: Standard deviation; VCMs: Vital capacity maneuvers.

**Supplementary Information**

The online version contains supplementary material available at https://doi.org/10.1186/s13019-021-01699-1.

**Additional file 1.** Protocol of VONTCPB.
Acknowledgements
We thank the Department of Cardiovascular Surgery, West China Hospital, Sichuan University for their support in the implementation of the trial.

Authors' contributions
MQZ, Hai Y: Study concept and design; MQZ, YQL, XFL, WS, WWJ, ZLW: Acquisition, Analysis or Interpretation of Data; MQZ, Hai Y: Drafting of Manuscript; Hai Y, Hong Y: Critical Revision of Manuscript; WS, XY: Administrative, technical or material support; All authors read and approved the final manuscript.

Funding
None.

Availability of data and materials
Data are available upon request.

Declarations

Ethics approval and consent to participate
The trial was approved by both institutional ethics committee and conducted in accordance with the Declaration of Helsinki (2013). The study was registered on Chinese Clinical Trial Registry (Registry number: ChiCTR1800015261). All patients provided written consent prior to enrollment.

Consent for publication
Not applicable.

Competing interests
The authors declare that they have no competing interests.

Author details
1 Department of Anesthesiology, West China Hospital, Sichuan University and The Research Units of West China (2018RU012), Chinese Academy of Medical Sciences, Chengdu 610041, China. 2 Department of Anesthesiology, The Third People's Hospital of Chengdu, Chengdu 610041, China.

Received: 25 May 2021 Accepted: 20 October 2021 Published online: 30 October 2021

References
1. Circulation CSOE. White book of Chinese cardiovascular surgery and extracorporeal circulation in 2019. Chin J Extracorporeal Circ. 2020;18(4):193–6.
2. Lagier D, Fischer F, Fornier W, et al. Effect of open-lung vs conventional perioperative ventilation strategies on postoperative pulmonary complications after on-pump cardiac surgery: the PROVECS randomized clinical trial. Intensive Care Med. 2019;45:1401–12.
3. Serpa Neto A, Hemmes SN, Barbas CS, et al. Incidence of mortality and morbidity related to postoperative lung injury in patients who have undergone abdominal or thoracic surgery: a systematic review and meta-analysis. Lancet Respir Med. 2014;2(12):1007–15.
4. Mathis MR, Duggal NM, Likosky DS, et al. Intraoperative mechanical ventilation and postoperative pulmonary complications after cardiac surgery. Anesthesiology. 2019;131:1046–62.
5. Wang YC, Huang CH, Tu YK. Effects of positive airway pressure and mechanical ventilation of the lungs during cardiopulmonary bypass on pulmonary adverse events after cardiac surgery: a systematic review and meta-analysis. J Cardiothoracic Vascular Anesth. 2018;32:748–59.
6. Bhatia M, Kidd B, Kumar PA. Pro: mechanical ventilation should be continued during cardiopulmonary bypass. J Cardiothoracic Vascular Anesth. 2018;32:1998–2000.
7. Dryer C, Tolin D, Antion J. Con: mechanical ventilation during cardiopulmonary bypass does not improve outcomes after cardiac surgery. J Cardiothoracic Vascular Anesth. 2018;32:2001–4.
8. Chi D, Chen C, Shi Y, et al. Ventilation during cardiopulmonary bypass for prevention of respiratory insufficiency: a meta-analysis of randomized controlled trials. Medicine. 2017;96:e6454.
9. Wahba A, Milojovic M, Boer C, et al. 2019 EACTS/EACTA/EBCP guidelines on cardiopulmonary bypass in adult cardiac surgery. Eur J Cardiothoracic Surg. 2020;57(2):210–31.
10. Heinrichs J, Grocott HP. Pro: hyperoxia should be used during cardiac surgery. J Cardiothoracic Vascular Anesth. 2019;33:2070–4.
11. Roberts SM, Cios TJ. Con: hyperoxia should not be used routinely in the management of cardiopulmonary bypass. J Cardiothoracic Vascular Anesth. 2019;33:2075–8.
12. Zhang MQ, Liao YQ, Yu H, et al. Ventilation strategies with different inhaled Oxygen conceNTration during CardioPulmonary Bypass in car‑diac surgery (VONTCPB): study protocol for a randomized controlled trial. Trials. 2019;20:254.
13. Bignami E, Guarnieri M, Saglietti F, et al. Mechanical ventilation during car‑diopulmonary bypass. J Cardiothoracic Vascular Anesth. 2016;30:1668–75.
14. Costa Leme A, Hajjar LA, Volpe MS, et al. Effect of intensive vs moderate alveolar recruitment strategies added to lung-protective ventilation on postoperative pulmonary complications: a randomized clinical trial. JAMA. 2017;317:422–32.
15. Cao J, Zhang S. Multiple comparison procedures. JAMA. 2014;312:543–4.
16. Fischer MO, Courteille B, Guinot PG, et al. Perioperative Ventilatory Management in Cardiac Surgery: A French Nationwide Survey. Medicine. 2016;95:e2655.
17. Tanner TG, Colvin MO. Pulmonary complications of cardiac surgery: Lung. 2020;198:889–96.
18. Beer L, Warszawskia JM, Schenk P, et al. Intraoperative ventilation strategy during cardiopulmonary bypass attenuates the release of matrix metalloproteinases and improves oxygenation. J Surg Res. 2015;195:294–302.
19. Nguyen LS, Estagnasie P, Merzoug M, et al. Low-tidal volume mechanical ventilation against no ventilation during cardiopulmonary bypass in heart surgery (MECANO): a randomized controlled trial. Chest 2020.
20. Hussain NS, Metry AA, Nakhlia GM, Wahba RM, Ragaee MZ, Bestarous JN. Comparative study between different modes of ventilation during cardiopulmonary bypass and its effect on postoperative pulmonary dysfunction. Anesth Essays Res. 2019;13:236–42.
21. Young CC, Harris EM, Vacciano C, et al. Lung-protective ventilation for the surgical patient: international expert panel-based consensus recommen‑dations. Br J Anesth. 2019;123:898–913.

Publisher’s Note
Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.