BMC Anesthesiology

RESEARCH

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Impact of zero-positive end-expiratory pressure on blood transfusion rates in off-pump coronary artery bypass surgery: a retrospective cohort study

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Abstract

Background Bleeding are common in cardiac surgery, with significant impacts on transfusion-related complications and patient prognosis. This study aimed to determine the differences in perioperative blood loss, transfusion rates, and the incidence of postoperative pulmonary complications (PPCs) with and without the use of positive end-expiratory pressure (PEEP) in patients undergoing off-pump coronary artery bypass graft surgery (OPCAB).

Methods This single-center, retrospective study included 106 adult patients undergoing coronary artery bypass surgery without cardiopulmonary bypass from January 2018 to March 2022. The patients were divided into two groups based on intraoperative ventilator settings: the zero-PEEP (ZEEP) group and the PEEP group. The primary outcome was the perioperative transfusion rate from the intraoperative period to postoperative 7 day. The incidence of PPCs was recorded for 1 week post-operatively. Logistic regression analysis was performed for statistical analysis.

Results The average PEEP in the PEEP group was 4.92 ± 0.42 cmH_2O. Multiple regression analysis indicated that lower mean airway pressure during surgery tend to associate with intraoperative lower blood loss. The intraoperative transfusion rates in the ZEEP group were significantly lower than those in the PEEP group (ZEEP:14%, PEEP 38.4%, $P=0.02$). Logistic regression analysis revealed that ZEEP (adjusted odds ratio [OR] 0.13, 95% confidence interval [CI] 0.04–0.78) and Society of Thoracic Surgeons(STS) scores (adjusted OR 2.31, 95% CI 1.53–3.49) were significantly associated with a reduced requirement for perioperative transfusions. No significant difference was observed between the two groups in terms of PPCs ($p=0.824$). Atelectasis was the most common complication in both groups (ZEEP: 35.7%, PEEP: 40%, $P=0.832$).

Conclusions ZEEP and STS scores were associated with significantly reduced requirement for perioperative transfusion rates during elective OPCAB surgery. However, ZEEP did not significantly affect the incidence of PPCs.

Keywords Coronary artery bypass, Off-pump, Positive end-expiratory pressure, Blood transfusion, Postoperative complications, Pulmonary atelectasis

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Background

Bleeding is the most common complication of cardiac surgery [1, 2], and consequent blood transfusions increase the risks of perioperative mortality, infection [3], and delirium. Therefore, the goal of perioperative management is to minimize and avoid blood transfusions. The primary strategies for reducing transfusions in cardiac surgery include preoperative interventions for anemia [4], intraoperative management of coagulation [5], and limiting the use of colloids [6]. The transfusion rates in coronary artery bypass grafting (CABG) have decreased from 50 to 19% [7] over the past two decades. Furthermore, although transfusion triggers have evolved over time [8], leading to changes in transfusion rates, CABG remains a procedure with a high transfusion demand.

Some studies have focused on minimizing the requirement for intraoperative bleeding through circulatory and respiratory control. For instance, zero-positive end-expiratory pressure (ZEEP) significantly reduced intraoperative bleeding and shortened the operative time during hepatectomy [9]. Furthermore, lowering the central venous pressure significantly reduces intraoperative bleeding [10]. Pressure control settings on the ventilator have been shown to significantly reduce blood loss compared with volume control during spinal surgery [11]. Thus, interventions to reduce intraoperative bleeding have been studied in several surgeries, however, to our knowledge such interventions have not been studied in cardiac surgery, despite the more common occurrence of bleeding and blood transfusions [7].

Positive end-expiratory pressure (PEEP) improves oxygenation by increasing the end-expiratory lung capacity, decreasing the pulmonary shunt rates, and increasing the balance between ventilation and blood flow [12]. However, randomized controlled trials of patients undergoing cardiac surgery with cardiopulmonary bypass have reported no association between high intraoperative PEEP and the incidence of postoperative respiratory complications (PPC) [13]. The incidence of PPCs during cardiac surgery is higher than that during non-cardiac surgery [14], leading to longer hospital stays and higher healthcare costs; thus, interventions, such as preoperative respiratory rehabilitation, are recommended to prevent the incidence of PPCs [15, 16]. However, there is insufficient evidence regarding intraoperative respiratory management.

This study aimed to determine the differences in perioperative blood loss, transfusion rates, and the incidence of PPCs with and without the use of PEEP in patients undergoing off-pump coronary artery bypass graft surgery (OPCAB), which requires a longer period of respiratory management than cardiopulmonary bypass. We hypothesized that ZEEP would reduce blood loss and transfusion rates in patients undergoing OPCAB.

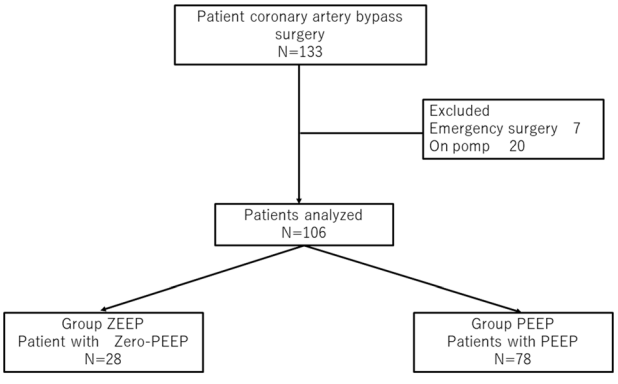

Fig. 1 Patient population. ECMO, extracorporeal membrane oxygenation. Patients undergoing coronary artery bypass surgery without cardiopulmonary bypass at a single hospital were excluded from the exclusion criteria. ECMO Conversion was defined as patients who required extracorporeal circulation due to intraoperative hemodynamic instability. Eligible patients for analysis were classified according to the type of end-expiratory positive pressure used

Methods

Study population

This retrospective observational study was approved by the Research ethics committee of the graduate school of medicine, Chiba university (♯M10313). The Institutional Review Board (Research Ethics Committee of the Graduate School of Medicine, Chiba University) determined that individual informed consent was not required for this retrospective study. Adult patients who underwent elective OPCAB under general anesthesia between January 2018 and March 2022 were included in this study. Patients undergoing emergency surgery, perioperative cardiopulmonary bypass, and cases with missing ventilator settings data were excluded. One hundred five patients were included in the analysis (Fig. 1). Patients who were intraoperatively converted to Extracorporeal Membrane Oxygenation (ECMO) were excluded. Emergency surgery and cases with missing data were excluded.

Anesthesia and surgical management

General anesthesia was introduced using 20–100 μg/kg of midazolam followed by 2–3 μg/kg of fentanyl and 0.1–0.2 μg/kg/min of remifentanil or 0.6–1 mg/kg of rocuronium. After tracheal intubation, anesthesia was maintained using sevoflurane or propofol in combination with remifentanil and fentanyl. Surgery was performed via sternotomy. An artery graft was obtained from the internal thoracic artery; grafts from the saphenous vein or radial artery were used, if required. Heparin was initially administered at a dose of 150 units/kg and increased to maintain an activated clotting time (ACT) of >250 s (Hemochron Jr. Signature® from Accriva Diagnostics, San Diego, CA, USA). Intraoperative hemorrhage

was collected via cell salvage, and the salvaged blood was returned, or red blood cells were transfused at a threshold of hemoglobin (Hb) 7.5–8 g/dL [17]. The fibrinogen concentration was monitored using the rapid dry hematology method: FibCare® (A&T Corporation, Kanagawa, Japan). Fresh-frozen plasma was transfused depending on the clinical bleeding tendency and a fibrinogen concentration of 150 mg/dL as a threshold value. Intraoperative coagulation management, which may be related to blood loss and transfusion rates, was excluded from the present analysis as all patients were managed using a common method based on the guidelines [5]. Tranexamic acid was basically administered at a dose of 20 mg/kg bolus and 10 mg/kg/hr continuous, and the dose was reduced according to body weight, renal function, and age under a unified protocol.

Respiratory management

All patients were ventilated at a tidal volume of 8–6 mg/kg of ideal body weight after tracheal intubation and maintained at a PEEP of 5–7 cmH_2O until the start of surgery. The mean airway pressure and peak airway pressure in the ventilator were continuously during surgery, and the median values were used. The Multi-gas Unit GF-300 Series® (NIHON KOHDEN CORPORATION, Tokyo, Japan) was employed. In the ZEEP group, PEEP was set to 0 at the start of the surgery and maintained until chest closure. Lung recruitment maneuvers (RMs) were performed at the time of stable hemodynamics during the procedure. The pressure control was set to 30 cmH2O with a 30-second inspiratory hold [18]. At the end of the RM, the respiratory rate, inspiratory/expiratory ratio, inspiratory hold, and tidal volume were returned to their previous values. In both groups, RMs were performed when oxygenation deteriorated, while monitoring hemodynamics. In the ZEEP group, RMs were performed in all patients after chest closure. Postoperative respiratory management was provided by a different team who were blinded to the intraoperative ventilation strategy, and the appropriate respiratory management method was selected based on the patient's background and respiratory status. The decision to use either ZEEP or PEEP during surgery was made by the attending anesthesiologist based on preoperative pulmonary function, cardiac function, and the anticipated surgical procedure.

Primary outcome

The primary outcome was perioperative transfusion rate, defined as the sum of the intraoperative transfusion rate and the transfusion rate during the first postoperative week. The perioperative transfusion rate did not include blood returned via cell salvage. The secondary endpoint was the incidence of pulmonary complications within 7 postoperative days and perioperative blood loss, defined as intraoperative blood loss and blood loss within the first 12 postoperative hours. Pulmonary complications were defined as follows [13]:

1. Mild respiratory failure: saturation of percutaneous oxygen (SpO_2)of < 90% or partial pressure of arterial oxygen (PaO_2) of < 60 mmHg after breathing ambient air (excluding hypoventilation) for 10 min and corrected with an oxygen supply of 1–3 L/min via a nasal cannula.
2. Moderate respiratory failure: SpO_2 of < 90% or PaO_2 of < 60 mmHg despite an oxygen supply of 3 L/min via a nasal cannula (excluding hypoventilation) and corrected with an oxygen supply of 4–10 L/min via a facemask.
3. Severe respiratory failure: SpO_2 of < 90% or PaO_2 of < 60 mmHg despite an oxygen supply of 10 L/min via a face mask (excluding hypoventilation) and corrected using an oxygen supply of > 10 L/min with a high-flow face mask, non-invasive ventilation, high-flow nasal oxygen therapy, or invasive mechanical ventilation.
4. Fast-track extubation failure associated with hypoxemia: delayed extubation after the first 6 postoperative hours associated with a PaO_2/fraction of inspired oxygen (FiO_2) of < 300.
5. New invasive mechanical ventilation associated with hypoxemia: PaO_2/FiO_2 of < 300.
6. Bronchospasm: new wheezing indicating the requirement for bronchodilator treatment (except for preoperative chronic obstructive pulmonary disease or asthma).
7. Severe tracheo-bronchial congestion: audible bronchi associated with disturbances in respiratory mechanics.
8. Post-extubation respiratory acidosis: pH of ≤ 7.30 and partial pressure of carbon dioxide ($PaCO_2$) of > 45 mmHg.
9. Pneumothorax: Presence of new pulmonary infiltrate on chest radiographs.
10. Pneumonia: new pulmonary infiltrate observed on a chest radiograph with at least two of the following: temperature of > 38.5 °C or < 35.5 °C, leukocytosis or leukopenia (white blood cell count of > 12,000 cells/mm^3 or < 4000 cells/mm^3), purulent secretions, and antibiotic treatment.
11. Pleural effusion requiring further postoperative pleural drainage.
12. Radiological atelectasis: new lung opacity observed on chest radiographs with a shift in the mediastinum or ipsilateral hemidiaphragm.
13. Acute respiratory distress syndrome (ARDS): as defined by the Berlin definition.

Statistical analysis

Parametric data were expressed as mean ± standard deviation (SD) for continuous variables and as frequencies and percentages for categorical variables. Nonparametric data were expressed as medians and quartiles. Group comparisons between patients with ZEEP and PEEP were performed using the Student's t-test or Mann-Whitney test for continuous variables and Fisher's exact test for categorical variables.

In primary analysis, multiple logistic regression analysis was used to determine the independent risk factors for the perioperative transfusion rate. Sample size calculation for the primary analysis determined that 83 cases would be required to detect a difference in transfusion rates between the PEEP group (50%) and ZEEP group (20%). Given the anticipated lower enrollment in the ZEEP group, an allocation ratio (ZEEP: PEEP) of 0.4 was applied, assuming a type I error (α) of 0.05 and power (1-β) of 0.8. As no previous studies have directly compared transfusion rates between PEEP and ZEEP groups, these proportions were estimated based on related literature [7]. For the logistic regression model incorporating three explanatory variables and assuming an overall transfusion rate of 35%, the required sample size was estimated at 100 cases [19]. The final study population comprised 106 cases, which exceeded the calculated sample size requirements. The Society of Thoracic Surgeons (STS) [20] score was used as a preoperative explanatory factor, while the use of PEEP (primary outcome) and colloid usage [5, 6] were included as intraoperative explanatory factors based on a literature review. In the secondary analysis, multiple regression analysis was conducted using log-transformed blood loss as the dependent variable, to normalize the distribution of the data, with the STS score, colloid use, and mean airway pressure (P mean) as explanatory variables. P-values were two-sided, with a value of less than 0.05 considered significant.

All statistical analyses were performed using R version 4.1.2. (R Foundation for Statistical Computing, Vienna, Austria) and G*Power Version 3.1.9.7 [21]. A statistical expert (A.N.) reviewed the statistical analyses performed in this study.

Results

A total of 106 patients were analyzed and selected based on the exclusion criteria outlined in Fig. 1. There were no significant differences in baseline characteristics between the two groups. Preoperative hemoglobin concentration, platelet counts, use of antiplatelet medications, and presence of coagulopathy before surgery were comparable between the groups (Table 1).

Intraoperative respiratory management

Twenty-eight patients were managed with ZEEP under ventilator settings, while the remaining patients were managed with PEEP at a mean pressure of 4.92 ± 0.42 cmH2O. Both P mean and P peak were significantly lower in the ZEEP group. (Fig. 2) No hypoxic events requiring intervention occurred in either group during the operation. In the multiple regression analysis with intraoperative blood loss as the dependent variable, the use of colloids and higher P mean tended to be associated with increased blood loss.(P=0.066, respectively)

Blood transfusion rate

The intraoperative transfusion rate was 4/28 (14%) in the ZEEP group and 30/78 (38.5%) in the PEEP group, demonstrating a significant difference ($p=0.02$). The total transfusion rate, including intraoperative transfusions and those within seven days postoperatively, was 6/28 (21.4%) in the ZEEP group and 34/78 (43.6%) in the PEEP group ($p=0.043$). The use of salvaged blood was similar between the two groups, with red blood cell transfusions being the most frequently administered. No significant differences were observed between the groups in terms of postoperative anemia, either immediately after surgery or the following day.

Primary outcome

Logistic multivariate analysis revealed that STS scores (adjusted odds ratio [OR]2.3, 95% confidence interval [CI] 1.53-3.49) and ZEEP management (adjusted OR 0.13, 95% CI 0.04-0.78) were significantly associated with perioperative blood transfusion rates (Table 2).

The use of colloids was significantly lower in the ZEEP group; however, intraoperative colloid use was not associated with perioperative transfusion rates in this analysis. The Hosmer–Lemeshow goodness-of-fit test for the logistic regression model showed no evidence of poor fit ($p=0.221$), and Nagelkerke's R^2 was 0.42.

Secondary outcome

Postoperative pulmonary complications (PPCs) occurred within seven days in 60.7% of patients in the ZEEP group and 56.4% of patients in the PEEP group, though the difference was not statistically significant ($p=0.824$). Atelectasis was the most common complication in both groups, occurring in 35.7% of the ZEEP group and 38.4% of the PEEP group ($p=0.832$) (Table 3).

Discussion

The present study demonstrates that the use of ZEEP is associated with lower perioperative blood transfusion rates in scheduled OPCAB procedures at a single center. Additionally, patients with higher STS scores were more likely to require perioperative blood transfusions.

Table 1 Patient characteristics and perioperative data with or without positive end-expiratory pressure

Demographics	ZEEP(*n* = 28)	PEEP(*n* = 78)	*p* value
Preoperative data			
Age, median (IQR)(yr)	70(62–84)	72(65–87)	0.307
Male, n (%)	25(89.3)	63(80.8)	0.389
Hight, median (IQR)(cm)	165(161–173)	165(158–168)	0.265
Body mass index, median (IQR)(kg/m2)	24.2(21.5–25.8)	23.8(21.1–25.4)	0.54
STS score, median (IQR)	1.24(0.25–2.34)	1.5(0.87–2.7)	0.231
ASA-PS, median (IQR)	3(3–3)	3(3–3)	0.71
NYHA, median (IQR)	1(1–2)	1(1–2)	0.378
Hypertension, n (%)	22(78.5)	55(70.5)	0.469
Hyperlipidemia, n (%)	16(57.1)	39(50)	0.66
Diabetes, n (%)	16(57.1)	43(55.1)	1
Hemodialysis, n (%)	5(17.9)	9(11.5)	0.515
COPD, n (%)	3(10.7)	4(5.1)	0.377
Hb, median (IQR)(g/dl)	13.2(11.7–15.1)	12.9(11.2–14.5)	0.125
Platelet, median (IQR)(10^3/μl)	217(177–242)	184(158–255)	0.195
Fibrinogen, median (IQR)(mg/dl)	334(303–380)	326(271–384)	0.488
APTT, median (IQR) (sec)	28(26.7–30.7)	29(27-31.1)	0.537
PT-INR, median (IOQ)	0.98(0.94–1.02)	0.97(0.95–0.99)	0.994
Creatinine, median (IQR)(mg/dl)	0.96(0.78–1.25)	0.94(0.78–1.24)	0.672
Smoking within 1month, n (%)	3(10.7)	6(7.7)	0.687
Smoking history, n (%)	15(53.6)	55(70.5)	0.165
Antiplatelet therapy, n (%)	14(50)	44(56.4)	0.659
Anticoagulant therapy, n (%)	5(17.9)	7(8.9)	0.294
Intraoperative management			
PEEP, median (IQR)(cmH2O)	0(0–0)	5(5–5)	< 0.001
P mean, median (IQR)(cmH2O)	6.7(5.6–7.5)	8.1(7.6–8.7)	< 0.001
P peak, median (IQR)(cmH2O)	11.8(10.7–12.7)	14(12.6–15)	< 0.001
Colloid, median (IQR)(ml)	0(0–0)	0(0-988)	0.017
Albumin, median (IQR)(ml)	0(0–0)	0(0-500)	0.195
Salvaged blood, median (IQR)(ml)	220(1-410)	230(0-583)	0.876
Transfusion, median (IQR)(ml)	300(150–750)	570(295–1100)	0.044
RBC transfusion, median (IQR), (ml)	0(0–0)	0(0-560)	0.033
FFP transfusion, median (IQR)(ml)	0(0–0)	0(0–0)	0.358
Platelet transfusion, median (IQR)(ml)	0(0–0)	0(0–0)	0.813
Transfusion, n (%)	4(14)	30(38.5)	0.02
Inhalation anesthesia, n (%)	27(96.4)	67(85.9)	0.176
Operation time, median (IQR)(min)	378(345–444)	375(340–434)	0.718
Intraoperative bleeding, median (IQR)(g)	1035(790–1545)	1280(791–1952)	0.342
Experience of surgeon < 15years, n (%)	2(7.1)	14(18)	0.227
Bypass site, median (IQR)	3(3–4)	4(3–4)	0.092
Graft site BITA, n (%)	19(67.9)	53(67.9)	1
SITA, n (%)	9(32.1)	25(32)	1
SVG, n (%)	19(67.9)	58(74.4)	0.622
RA, n (%)	14(50)	35(44.9)	0.665
Postoperative complication			
Postoperative transfusion, n (%)	4(14)	16(20.5)	0.58
Total transfusion, n (%)	6(21.4)	34(43.6)	0.043
Postoperative Hb, median (IQR)(g/dl)	10.4(9.3–11.3)	9.9(9-10.8)	0.13
POD 1 Hb, median (IQR)(g/dl)	10(8.8–11)	9.9(9.4–10.8)	0.725
Pulmonary complications, n (%)	17(60.7)	44(56.4)	0.824

IQR,; STS, Society of Thoracic Surgeons; ASA-PS, American Society of Anesthesiologists physical status; NYHA, New York Heart Association; COPD, chronic obstructive pulmonary disease; Hb, Hemoglobin; PT, Prothrombin Time; APTT, Activated Partial Thromboplastin Time; PEEP, positive end expiratory pressure; P mean, airway pressure mean; P peak, airway pressure peak; RBC, Red blood cell; FFP, Fresh frozen plazma; BITA, Bilateral Internal Thoracic Artery; SITA, Single Internal Thoracic Artery; SVG, Saphenous Vein Graft; RA, Radial Artery; POD, Postoperative Day

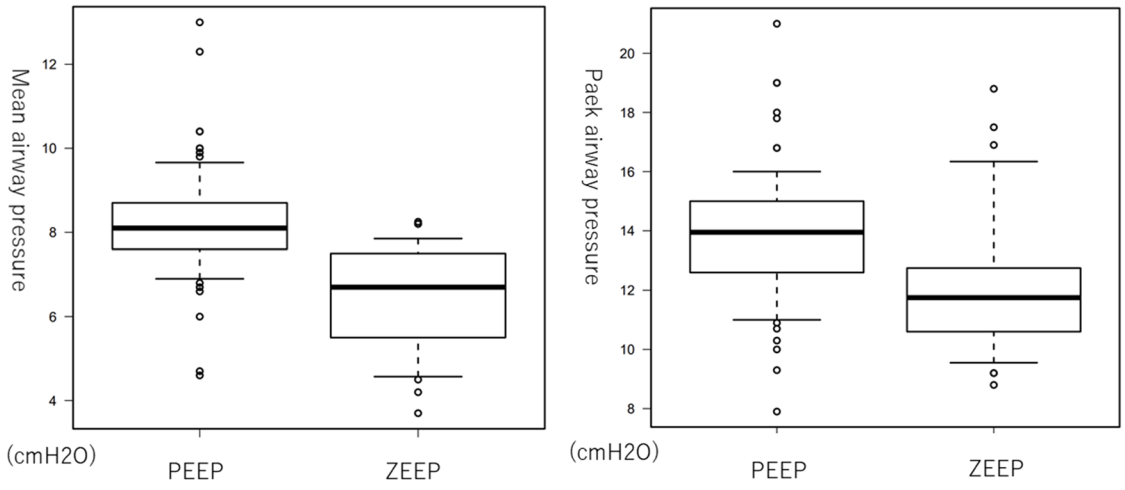

Fig. 2 Comparison of mean and peak airway pressures between the Zero End-Expiratory Pressure (ZEEP) group and the Positive End-Expiratory Pressure (PEEP) group. ZEEP, Zero End-Expiratory Pressure; PEEP, Positive End-Expiratory Pressure. The graph illustrates the comparison of mean and peak airway pressures between the two groups, with the vertical axis representing the airway pressures. The PEEP group shows significantly higher values in both mean and peak airway pressures compared to the ZEEP group

Table 2 Result of the logistic regression analysis

	Adjusted Odds Ratio	95% Confidence interval	*P* value
STS score	2.31	1.53–3.49	< 0.001
ZEEP	0.13	0.04–0.78	0.021
Colloid	0.59	0.22–1.62	0.306

OR, Odds Ratio; CI, confidence interval; STS, Society of Thoracic Surgeons; ZEEP, zero-positive end-expiratory pressure

Table 3 Postoperative pulmonary complication with or without positive end-expiratory pressure

	ZEEP (*n* = 28)	PEEP (*n* = 78)	relative risk	*p* value
Total	17(60.7)	44(56.4)	1.07	0.824
Mild respiratory failure	1(3.6)	2(2.5)	1.44	1
Moderate respiratory failure	1(3.6)	3(3.8)	0.95	1
Severe respiratory failure	5(17.9)	5(6.4)	2.8	0.137
Fast-track extubation failure	6(21.4)	11(14.1)	1.52	0.382
New invasive mechanical ventilation	0	0		
Bronchospasm	0	0		
Severe tracheo-bronchial congestion	0	0		
Post-extubation respiratory acidosis	0	0		
Pneumothorax	3(10.7)	2(2.6)	4.12	0.117
Pneumonia	0	0		
Pleural effusion with need for further postoperative pleural drainage	1(3.6)	6(7.7)	0.47	0.672
Atelectasis	10(35.7)	30(38.4)	0.93	0.832
ARDS	0	0		

ZEEP, zero-positive end-expiratory pressure; PEEP; positive end expiratory pressure; CI, confidence interval; ARDS, acute respiratory distress syndrome

Importantly, intraoperative ZEEP was not significantly associated with an increased incidence of respiratory events or complications during the first postoperative week.

While ZEEP showed a significant association with reduced perioperative transfusion rates in OPCAB, it is important to note that the relationship between ZEEP-induced reductions in central venous pressure (CVP) and decreased blood loss has been well-established in hepatic resection [10]. Similar to hepatectomy, cardiac surgery often involves substantial bleeding from the venous system. This is the first study ever to examine ZEEP in OPCAB in relation to bleeding and transfusion. Previous studies have reported that a significant correlation between CVP and PEEP persists in cardiac surgery, even following thoracotomy [22]. Our findings suggest that managing CVP with ZEEP may be an effective strategy to reduce both transfusion volume and blood loss during OPCAB procedures. Although the present study was unable to directly show the impact on CVP due to artifacts, the observed association between P mean and blood loss implies a potential influence of respiratory management on venous pressures.

Conversely, the lack of a significant association between ZEEP and blood loss in our study suggests that patient background factors and operative time may have had a greater impact on blood loss. Nonetheless, there was a trend toward less blood loss with lower P mean, and the reduction in P mean achieved with ZEEP may have contributed to the observed decreases in both blood loss and transfusion volume. Regarding red blood cell transfusion thresholds, although standardization was not achieved due to the retrospective nature of the study, hemoglobin

levels at three time points—preoperatively, at the end of surgery, and on the first postoperative day—showed no significant differences between the two groups. This suggests that transfusion decisions were made based on the thresholds adopted by each institution [17].

The use of PEEP, especially at higher levels, can cause hypotension and an increased need for vasopressor drugs [23], colloids and blood transfusions. Since minimizing hypotension due to cardiac displacement during OPCAB surgery is critical, the use of ZEEP may help prevent hypotension and reduce the need for colloids and blood transfusions. This may, in turn, lower the risk of dilutional coagulopathy [6]. The ability to maintain coagulation function intraoperatively by limiting colloid and red blood cell transfusions in the ZEEP group may have contributed to the observed reduction in both intraoperative and postoperative transfusion rates.

In cardiac surgery, the open lung strategy during cardiopulmonary bypass has not been associated with an increased incidence of PPCs, although elevated intraoperative plasma concentrations of biomarkers indicative of lung injury were observed in the high-PEEP group [24]. Similarly, in our study, there was no significant difference in the incidence of postoperative pulmonary complications between the ZEEP and PEEP groups, and the incidence was consistent with previously reported rates of PPCs in cardiac surgery [14]. In contrast to previous findings where peak pressures gradually increased in the ZEEP group towards the end of hepatectomy [25], our study demonstrated that both P mean and P peak were significantly lower in the ZEEP group. The negative impact of ZEEP on respiratory function and lung injury during surgery were considered to be minimal.

PEEP is a widely recognized technique for improving perioperative oxygenation, and lung-protective ventilation combined with PEEP and low-minute volume ventilation has been shown to reduce postoperative respiratory complications. However, insufficient effectiveness often exists without optimizing the level of PEEP [12, 26].

In addition, the improvement in lung aeration by PEEP tends to disappear 15 min after extubation compared to the end of surgery [27], emphasizing the need for continued use of PEEP after extubation to maintain its effectiveness. There is no conclusive evidence that PEEP alone reduces the incidence of postoperative pulmonary complications in patients undergoing major surgery, including obese patients [27–31]. Furthermore, although many studies focusing on PEEP have used PPCs as the primary outcome [28, 30–32], other factors such as intraoperative hypotension, increased central venous pressure (CVP), surgical bleeding, and transfusion rates should also be considered in the comprehensive management of perioperative patients.

Limitations

First, this study has inherent limitations associated with its single-center, retrospective cohort design. As a teaching hospital setting, there may be selection bias due to the involvement of multiple surgeons and anesthesiologists with varying levels of experience and clinical preferences. Although our institutional standardized protocols for anesthesia management and surgical procedures helped minimize practice variability, potential differences in transfusion thresholds and recruitment maneuver implementation could not be completely eliminated due to the retrospective nature of the study. To establish more generalizable findings and address these limitations, multicenter prospective studies with standardized protocols are necessary.

Second, unmeasured confounding is a concern, particularly regarding the decision to apply ZEEP. However, no significant differences were observed in baseline patient characteristics, including STS scores, NYHA classifications, and the presence of COPD. To obtain more robust evidence, a randomized controlled trial (RCT) is necessary to address this limitation.

Third, the study did not analyze ventilator management beyond PEEP and airway pressure. Future studies should incorporate protocols that include additional ventilator settings, such as tidal volume and ventilator mode. However, in this study, lung-protective ventilation with a tidal volume of 8 ml/kg or less [33] was consistently used in both groups, which is expected to have minimized the impact on PPCs.

Fourth, the retrospective design of this study precluded the accurate measurement of CVP. Consequently, we were unable to assess the impact of ZEEP on CVP or elucidate the mechanisms underlying the reduction in transfusion rates. Prospective studies specifically addressing these aspects are warranted.

Fifth, this study did not evaluate long-term outcomes. Given that transfusion strategies in cardiac surgery are associated with long-term prognosis [34], future large-scale trials should investigate the impact of ZEEP on long-term clinical outcomes.

Conclusion

Intraoperative ZEEP technique and STS score were significantly associated with perioperative blood transfusion rates in patients undergoing OPCAB surgery without increasing the incidence of PPCs.

Abbreviations

CABG	Coronary artery bypass grafting
ZEEP	Zero-positive end-expiratory pressure
PEEP	Positive end-expiratory pressure
PPCs	Postoperative respiratory complications
OPCAB	Off-pump coronary artery bypass graft surgery
ACT	Activated clotting time
SpO2	Saturation of percutaneous oxygen

PaO2	Partial pressure of arterial oxygen
FiO2	Fraction of inspired oxygen
PaCO2	Partial pressure of carbon dioxide
ARDS	Acute respiratory distress syndrome
SD	Standard deviation
STS	Society of Thoracic Surgeons
CI	Confidence interval
OR	Odds ratio

Acknowledgements
Not applicable.

Author contributions
All authors contributed significantly to this study. K.T. conceived and designed the study. K.T., S.K., and A.N. performed the statistical analyses. S.K., K.T., Y.I., and M.H-M wrote the manuscript. K.T., S.K., and Y.I. collected the data. All authors reviewed and approved the final version of the manuscript.

Funding
This study was supported by a Grant-in-Aid for Early-Career Scientists (23K15593) from the Japan Society for the Promotion of Science (Kyongsuk Son).

Data availability
Data cannot be shared openly but are available on request from authors: The data that support the findings of this study are not openly available due to reasons of sensitivity and are available from the corresponding author upon reasonable request.

Declarations

Ethics approval and consent to participate
The Institutional Review Board (Research Ethics Committee of the Graduate School of Medicine, Chiba University) approved the study protocol (#M10313) and waived the requirement for individual informed consent due to the retrospective nature of the study. Instead, an opt-out approach was implemented, with study details and the option to decline participation disclosed on the hospital's website. This ensured patient autonomy and compliance with ethical guidelines for retrospective studies. The study was conducted in accordance with the Clinical Trials Act of Japan and the Declaration of Helsinki.

Consent for publication
Not Applicable.

Competing interests
The authors declare no competing interests.

Received: 11 October 2024 / Accepted: 9 December 2024
Published online: 19 December 2024

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