ANESTHESIOLOGY

Intraoperative Mechanical Ventilation and Postoperative Pulmonary Complications after Cardiac Surgery

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EDITOR'S PERSPECTIVE

What We Already Know about This Topic

- Modern ventilation approaches use a bundle of lower tidal volumes, lower driving pressures, and positive end-expiratory pressure
- The contributions of each component to reducing postoperative pulmonary complications in an adult cardiac surgical population is not known

What This Article Tells Us That Is New

- In this retrospective analysis, the intraoperative ventilation bundle was associated with a lower rate of postoperative pulmonary complications
- Lower modified driving pressure was independently associated with fewer pulmonary complications

ABSTRACT

Background: Compared with historic ventilation strategies, modern lung-protective ventilation includes lower tidal volumes (V_T), lower driving pressures, and application of positive end-expiratory pressure (PEEP). The contributions of each component to an overall intraoperative protective ventilation strategy aimed at reducing postoperative pulmonary complications have neither been adequately resolved, nor comprehensively evaluated within an adult cardiac surgical population. The authors hypothesized that a bundled intraoperative protective ventilation strategy was independently associated with decreased odds of pulmonary complications after cardiac surgery.

Methods: In this observational cohort study, the authors reviewed nonemergent cardiac surgical procedures using cardiopulmonary bypass at a tertiary care academic medical center from 2006 to 2017. The authors tested associations between bundled or component intraoperative protective ventilation strategies (V_T below 8 ml/kg ideal body weight, modified driving pressure [peak inspiratory pressure – PEEP] below 16 cm H_2O, and PEEP greater than or equal to 5 cm H_2O) and postoperative outcomes, adjusting for previously identified risk factors. The primary outcome was a composite pulmonary complication; secondary outcomes included individual pulmonary complications, postoperative mortality, as well as durations of mechanical ventilation, intensive care unit stay, and hospital stay.

Results: Among 4,694 cases reviewed, 513 (10.9%) experienced pulmonary complications. After adjustment, an intraoperative lung-protective ventilation bundle was associated with decreased pulmonary complications (adjusted odds ratio, 0.56; 95% CI, 0.42–0.75). *Via* a sensitivity analysis, modified driving pressure below 16 cm H_2O was independently associated with decreased pulmonary complications (adjusted odds ratio, 0.51; 95% CI, 0.39–0.66), but V_T below 8 ml/kg and PEEP greater than or equal to 5 cm H_2O were not.

Conclusions: The authors identified an intraoperative lung-protective ventilation bundle as independently associated with reduced pulmonary complications after cardiac surgery. The findings offer insight into components of protective ventilation associated with adverse outcomes and may serve as targets for future prospective interventional studies investigating the impact of specific protective ventilation strategies on postoperative outcomes after cardiac surgery.

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Postoperative pulmonary complications, a well-documented group of complications after cardiac surgery, are associated with a fourfold increase in mortality,[1,2] extended intensive care unit (ICU) and hospital lengths of stay,[2,3] and more than $20,000 in institutional expenses per event.[3–5] In the cardiac surgery population, measurable derangements in pulmonary function occur in nearly all patients,[6,7] and approximately 10% to 25% develop postoperative pulmonary complications requiring substantial healthcare resource utilization.[1,6]

Cardiopulmonary bypass (CPB), mechanical ventilation, and surgical manipulation of the thoracic cavity each

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play major roles in the evolution of pulmonary injury.[1] Preoperative, intraoperative, and postoperative factors impact a patient's ability to cope with these insults.[7,8] Several externally validated risk scores incorporating these factors have been developed to improve risk stratification for postoperative pulmonary complications after cardiac surgery.[9,10] Despite rigorous model development, shortcomings of postoperative pulmonary complication prediction models remain evident. One recent multicenter study demonstrated that a large proportion of variation in pneumonia rates remains unexplained by prediction models focused on surgical technique and underlying patient risk, suggesting that other unmeasured practices may account for the differences observed.[11] One such process of care associated with postoperative pulmonary complications, yet not accounted for in current prediction models, is the practice of intraoperative lung-protective ventilation. Compared with historic intraoperative ventilation techniques, modern lung-protective ventilation strategies use lower tidal volumes (V_T),[1,4,5,12–15] lower driving pressures,[16–18] and positive end-expiratory pressure (PEEP).[13,15,19] These techniques have already gained acceptance in ICUs after large studies have demonstrated reduced morbidity and mortality.[18,20] However, the contributions of each component to an overall intraoperative lung-protective ventilation strategy aimed at reducing postoperative pulmonary complications (postoperative pulmonary complications) have not been comprehensively studied in an adult cardiac surgical population.

Although ICU ventilation after cardiac surgery has been assessed,[21,22] scarce data currently exist evaluating the relationship between intraoperative ventilator management during cardiac surgery, postoperative pulmonary complications, and mortality. Because the post-CPB intraoperative period represents a unique transition from often nonventilated to ventilated lungs, optimizing respiratory mechanics to reduce lung injury is of critical concern. To better characterize this currently understudied relationship, we performed an observational cohort study using the Society of Thoracic Surgeons and Multicenter Perioperative Outcomes Group databases at our institution. We hypothesized that a bundled intraoperative lung-protective ventilation strategy (*i.e.*, lower V_T, driving pressure, and application of PEEP) was independently associated with decreased odds of postoperative pulmonary complications after cardiac surgery, when adjusted within a novel, robust multivariable model leveraging data uniquely available from each database. We additionally hypothesized that when studied as separate exposures, components of the intraoperative bundled lung-protective ventilation strategy had differential associations with postoperative pulmonary complications.

Materials and Methods

We obtained Institutional Review Board approval (HUM00132314) for this observational cohort study performed at our academic quaternary care center; the requirement for informed patient consent was waived. We adhered to the Strengthening the Reporting of Observational Studies in Epidemiology checklist for reporting observational studies. Study methods including data collection, outcomes, and statistical analysis were established prospectively and presented at an institutional peer-review committee on January 20, 2016; a revised finalized proposal was registered before accessing study data.[23]

Patient Population

Inclusion criteria for the study were adult (at least 18 yr old) patients who underwent elective or urgent cardiac surgical procedures with full CPB, limited to coronary artery bypass grafting, valve, and aortic procedures, performed in isolation or in combination. We reviewed patients over a continuous 11-yr study period from January 1, 2006 to June 1, 2017. Exclusion criteria were preoperative mechanical ventilation within 60 days of surgery, use of a double-lumen endotracheal tube or one-lung ventilation, American Society of Anesthesiologists class V or VI physical status, preoperative extracorporeal membrane oxygenation support, ventricular assist device implantation procedures (planned and unplanned), reoperative cardiac surgical procedures, transcatheter procedures, or procedures using partial- or left-heart bypass. At our institution, surgical techniques for the study cohort commonly included direct aortic cannulation *via* full sternotomy, and rarely, axillary or femoral cannulation or direct cannulation *via* mini-sternotomy. No robotic procedures or minimally invasive direct coronary artery bypass procedures were performed.

Data Collection

We collected study data from three sources: the Multicenter Perioperative Outcomes Group electronic anesthesia database, the Society of Thoracic Surgeons Adult Cardiac Surgery Database, and our hospital enterprise electronic health record. Within the Multicenter Perioperative Outcomes Group database, physiologic monitors including vital signs and ventilator settings and measurements are collected in automated fashion every 60 s and stored in an electronic intraoperative anesthesia record for all cases. Templated intraoperative script elements—including case times, medications and fluids administered, and anesthetic interventions such as airway management techniques—are additionally routinely recorded within the anesthesia record for all cases. Within the Society of Thoracic Surgeons database, patient history, surgical procedure, and outcome data are similarly stored as discrete concepts for all adult cardiac surgical procedures performed within our institution. To maintain high rates of interobserver agreement across cases, data are standardized using detailed prespecified definitions, and are collected (Society of Thoracic Surgeons database)[24] or validated (Multicenter Perioperative Outcomes Group database) by nurses with completed training in data definitions used. Detailed methods for data entry, validation,

and quality assurance are described elsewhere,[25–27] and have been used for multiple published studies.[28–31] Within the Multicenter Perioperative Outcomes Group and Society of Thoracic Surgeons databases, local datasets were linked *via* unique codified surgical case and patient identifiers; data extraction and analysis were performed on a secure server. Finally, local electronic health record data (Epic Systems Corporation, USA) were used to determine postoperative arterial blood gas values and ICU ventilator data, as necessary for components of outcome variables described below; these data were similarly linked to the final analytic dataset. The quality of local electronic health record data used for this study was verified *via* manual review by an anesthesiologist investigator (M.R.M.) of all cases experiencing the primary outcome, all cases with outlier data, and 10% of cases not experiencing the primary outcome.

Clinical Processes of Care

Perioperative anesthetic management for all cases was at the discretion of the attending cardiac anesthesiologist, who directs an anesthesia care team of anesthesiology fellows and residents. Routinely, anesthetic agents included induction with midazolam, propofol, or etomidate; analgesia with fentanyl or morphine; neuromuscular blockade with rocuronium, vecuronium, or cisatracurium; and maintenance with isoflurane, transitioned to a propofol or dexmedetomidine infusion before transport to ICU. In addition to standard monitoring, intraoperative hemodynamic management was routinely guided by invasive arterial line, central venous pressure, and pulmonary artery catheter monitors, as well as transesophageal echocardiography and arterial/mixed venous blood gas measurements. Fluids, blood products, vasoactive infusions, and inotropic infusions were managed at the discretion of the attending anesthesiologist in communication with the cardiac surgeon, with typical hemodynamic targets including a mean arterial pressure greater than 65 mmHg, cardiac index greater than 2.2 l/min/m^2, mixed venous oxygen saturation greater than 65%, hematocrit greater than 21%, and echocardiographic assessment of post-CPB ventricular systolic function unchanged to improved compared with pre-CPB function.

Ventilator settings in the operating room were managed by the attending anesthesiologist. Intubation was performed with a 7.5- or 8.0-mm-internal-diameter endotracheal tube. Mechanical ventilation was performed using Aisys CS2 anesthesia workstations (General Electric Healthcare, USA). Providers typically employed a pressure-controlled volume-guaranteed ventilation mode (default setting) throughout the entire study period, targeting normocapnia or mild hypocapnia, and avoiding hypoxemia. Of note, default settings on ventilators used included V_T = 500 ml and PEEP = 0 cm H_2O; the default PEEP setting was subsequently changed to PEEP = 5 cm H_2O in March 2007. Ventilation was paused during CPB; the ventilator circuit remained connected to the patient, but with no application of PEEP. Before discontinuation of CPB, it was resumed after providing recruitment maneuvers. After transport to ICU, a structured handoff detailing intraoperative management, including final ventilator settings and plan for extubation, was communicated to an ICU team of intensivists, nurses, and respiratory therapists. Ventilator weaning, extubation, and management of complications were made at the discretion of the ICU team, as based on local protocols and targeting goals discussed during postoperative handoff.

Outcomes

The primary outcome was occurrence of a postoperative pulmonary complication, predefined as a composite of pulmonary complications recorded in the Society of Thoracic Surgeons database and adjudicated by nurses trained in outcome definitions, or recorded in our enterprise electronic health record and adjudicated by an anesthesiologist (M.R.M.). These included any one of the following: prolonged initial postoperative ventilator duration longer than 24 h (Society of Thoracic Surgeons database), pneumonia (Society of Thoracic Surgeons database), reintubation (Society of Thoracic Surgeons database), or postoperative partial pressure of oxygen to fractional inspired oxygen (PaO_2/FIO_2) below 100 mmHg within 48 h postoperatively while intubated (local electronic health record, Appendix 1).

We selected a threshold of PaO_2/FIO_2 below 100 mmHg as a postoperative pulmonary complication component based on previously validated assessments of pulmonary dysfunction associated with mortality after cardiac surgery.[32–34] Given varied mechanisms of pulmonary injury, and the distinction between pneumonia *versus* other pulmonary complications as described in recent consensus guidelines,[35,36] each component of the postoperative pulmonary complication composite outcome was also separately analyzed as a secondary outcome. Additional predefined secondary outcomes included 30-day postoperative mortality, initial postoperative mechanical ventilation duration, minimum PaO_2/FIO_2 within 48 h postoperatively while intubated (as a continuous variable), length of ICU stay, and length of hospital stay. All secondary outcomes were similarly adjudicated by trained Society of Thoracic Surgeons nurse reviewers with the exception of minimum PaO_2/FIO_2 which was adjudicated by an anesthesiologist (M.R.M.).

Exposure Variables – Lung-protective Ventilation

The primary exposure variable studied was a bundled intraoperative lung-protective ventilation strategy, comprising median V_T below 8 ml/kg predicted body weight and median driving pressure below 16 cm H_2O and median PEEP at or above 5 cm H_2O. Varying lung-protective cutoffs for each ventilator component are currently described in the literature, ranging from V_T 6 to 10 ml/kg predicted body weight,[1,13,15] driving pressure 8 to 19 cm H_2O,[16,18,37] and PEEP 3 to 12 cm H_2O.[13,15] Given these ranges, our

cutoffs were selected by inspection of previously collected ventilation practice institutional data, targeting upper quartiles (approximately 75% compliance for each component) to ensure class balance between cases with lung-protective ventilation *versus* non-lung-protective ventilation and to improve multivariable model discrimination.[5,13,28,38–40]

Predicted body weight (in kg) was calculated as: 50 + 2.3 • (height [in] − 60) for men; 45 + 2.3 • (height [in] − 60) for women.[41] Modified airway driving pressure was calculated as (peak inspiratory pressure − PEEP). As performed in previous studies,[42] we used modified driving pressure for all cases, given the lack of ventilator plateau pressure data available within our electronic medical record necessary for a true driving pressure calculation. To adjust for decisions to maintain normoxia rather than a lung-protective ventilation strategy (otherwise favoring lower F_{IO_2} and moderate PEEP), intraoperative oxygen saturation measured by pulse oximetry and F_{IO_2} were included as covariates. To summarize each ventilator variable on a per-case basis, median values while mechanically ventilated were calculated. Ventilator parameters while on CPB, during which ventilators were routinely paused, were excluded from the median value calculation. For descriptive purposes, ventilator parameters were additionally subdivided into median value pairs, separated into the pre-CPB and post-CPB periods. In cases with multiple instances of CPB, post-CPB ventilator parameters were analyzed after the final CPB instance.

Covariate Data

For descriptive purposes and to adjust for confounding variables potentially associated with the exposure variables or study outcomes, a range of perioperative characteristics were included as covariates within our study. Patient anthropometric, medical history, anesthetic, surgical, and laboratory testing/study variables were selected as available within the Multicenter Perioperative Outcomes Group and Society of Thoracic Surgeons databases. All variables used in several existing scores for calculating risk of complications including postoperative pulmonary complications after cardiac surgery were included (*e.g.*, cardiac surgery type, bypass times, comorbidities, *etc.*), in addition to other relevant descriptive covariates (table 1).[9,10,43] To evaluate for changes in practice and Society of Thoracic Surgeons database reporting over the study time period, the Society of Thoracic Surgeons Adult Cardiac Surgery Database version was included as a covariate; this resulted in four time periods for adjustment (1/1/2006–12/31/2007; 1/1/2008–6/30/2011; 7/1/2011–6/30/2014; 7/1/2014–5/31/2017) To account for variation in unmeasured intraoperative practices attributable to the attending anesthesiologist and potentially associated with postoperative pulmonary complications, we characterized attending anesthesiologists by tertiles of low/medium/high frequency of bundled intraoperative lung-protective ventilation use.

Statistical Analysis

All statistical analyses were performed using SAS version 9.3 (SAS Institute, USA). Normality of continuous variables was graphically assessed using histograms and Q-Q plots. Continuous data were presented as mean ± SD or median and interquartile range; binary data were summarized via frequency and percentage. Comparisons of continuous data were made using a two-tailed independent *t* test or a Mann–Whitney *U* test, and categorical data were compared by a Pearson chi-square or Fisher's exact test, as appropriate. Trend analyses of the components of the lung-protective ventilation bundle were completed using the Cochran–Armitage test. A *P* value less than 0.05 denoted statistical significance.

Before any multivariable analysis, collinearity among covariates was assessed using the variance inflation factor; variables with a variance inflation factor greater than 10 were excluded. To target development of a clinically usable reduced-fit postoperative pulmonary complication multivariable model avoiding overfitting, covariates meaningfully describing the study population but not used in existing cardiac surgery risk score models were additionally excluded from multivariable analysis. Missing data were handled via a complete case analysis. To further aid in covariate selection, we used the least absolute shrinkage and selection operators technique and restricted covariates to the number of outcomes divided by 10, while also accounting for the lung-protective ventilation bundle as well as lung-protective ventilation bundle components (V_T, driving pressure, and PEEP). We chose this variable selection technique, given its ability to perform regularization and variable selection to improve model accuracy and interpretability, particularly among analyses with a relatively large number of covariates and modest number of outcomes.[44] Using a multivariable logistic regression model, we characterized the risk-adjusted association between the primary exposure of intraoperative lung-protective ventilation bundle and the primary outcome of postoperative pulmonary complication. Additionally, we repeated our multivariable analysis to assess independent associations between each lung-protective ventilation bundle component and postoperative pulmonary complications. Overall model discrimination of logistic regression models was assessed using the c statistic. Secondary outcomes were assessed using multivariable linear regression models. Goodness-of-fit for linear regression models was summarized via R-squared; such models were evaluated using varied distributional assumptions (*i.e.*, linear *versus* logarithmic transformations) for continuous secondary outcomes. Multilevel modeling clustering at the provider level was not possible because of limited sample size per provider; instead, the previously mentioned fixed covariate of anesthesiology attending lung-protective ventilation frequency tertile was used.

In addition to analyzing independent associations between an overall lung-protective ventilation strategy and

Table 1. Perioperative Patient Characteristics and Univariate/Bivariate Associations with Postoperative Pulmonary Complications

Characteristic	Entire Cohort N = 4694 n (%) or Mean ± SD/Median [Interquartile Range]	Postoperative Pulmonary Complication		*P* Value	% Cases with Complete Data
		No, N = 4181 (89.1%) n (%) or Mean ± SD/Median [Interquartile Range]	Yes, N = 513 (10.9%) n (%) or Mean ± SD/Median [Interquartile Range]		
Preoperative characteristics					
Age	62 ± 14	62 ± 14	64 ± 14	< .0001	100
Sex, male	3,024 ± 64.4	2,730 ± 65.3	294 ± 57.3	0.0004	100
Race, non-white	515 ± 11.0	442 ± 10.6	73 ± 14.2	0.0127	99.9
Height, cm	172 ± 11	172 ± 10	170 ± 11	< .0001	100
Actual body weight, kg	86.9 ± 21.0	87.0 ± 20.8	85.8 ± 22.8	0.2624	100
Predicted body weight, kg	65.8 ± 11.1	66.1 ± 11.0	63.6 ± 11.6	< .0001	100
Body mass index, kg/m^2				0.1389	100
Underweight (< 18.5)	52 ± 1.1	45 ± 1.1	7 ± 1.4		
Normal weight (18.5–24.9)	1,090 ± 23.2	971 ± 23.2	119 ± 23.2		
Overweight (25–29.9)	1,724 ± 36.7	1,551 ± 37.1	173 ± 33.7		
Class I obesity (30–34.9)	1,065 ± 22.7	954 ± 22.8	111 ± 21.6		
Class II obesity (35–39.9)	448 ± 9.5	392 ± 9.4	56 ± 10.9		
Class III obesity (≥ 40)	315 ± 6.7	268 ± 6.4	47 ± 9.2		
Current smoker	630 ± 13.4	551 ± 13.2	79 ± 15.4	0.1637	100
Chronic lung disease*	543 ± 11.6	444 ± 10.6	99 ± 19.3	< .0001	100
Recent pneumonia within one month	55 ± 1.2	45 ± 1.1	10 ± 2.0	0.0829	100
Sleep apnea	490 ± 10.4	442 ± 10.6	48 ± 9.4	0.3957	100
Pulmonary hypertension	1,447 ± 30.8	1,296 ± 31.0	151 ± 29.4	< .0001	99.5
Moderate (PA systolic pressure 31–55 mmHg)	1,185 ± 25.2	1,088 ± 26.1	97 ± 19.1		
Severe (PA systolic pressure > 55 mmHg)	262 ± 5.6	208 ± 5.0	54 ± 10.7		
New York Heart Association Class				< .0001	99.0
I	3,807 ± 81.9	3,448 ± 83.3	359 ± 70.8		
II	305 ± 6.6	272 ± 6.6	33 ± 6.5		
III	409 ± 8.8	326 ± 7.9	83 ± 16.4		
IV	125 ± 2.7	93 ± 2.3	32 ± 6.3		
Recent myocardial infarction < 21 days	329 ± 7.0	275 ± 6.6	54 ± 10.5	0.0009	100
Preoperative left ventricular ejection fraction, %	60 [55, 65]	60 [55, 65]	60 [50, 65]	0.0003	100
Poor mobility†	2,353 ± 50.1	2,030 ± 48.6	323 ± 63.0	< .0001	100
Extracardiac arteriopathy	931 ± 19.8	798 ± 19.1	133 ± 25.9	0.0002	100
Peripheral arterial disease	333 ± 7.1	278 ± 6.7	55 ± 10.7	0.0007	
Carotid disease	602 ± 12.8	519 ± 12.4	83 ± 16.2	0.0161	
Amputation for arterial disease	69 ± 1.5	57 ± 1.4	12 ± 2.3	0.0830	
Previous major vascular surgical intervention	224 ± 4.8	188 ± 4.5	36 ± 7.0	0.0115	
Dyslipidemia	2,703 ± 57.6	2,419 ± 57.9	284 (55.4)	0.2803	100
Arrhythmia‡	735 ± 15.7	626 ± 15.0	109 ± 21.3	0.0002	100
Renal Impairment					
Creatinine clearance, ml · min^{-1} · 1.73 m^{-2}§	76.5 ± 24.5	77.9 ± 23.8	65.2 ± 27.4	< .0001	99.8
Dialysis requirement	104 ± 2.2	72 ± 1.7	32 ± 6.2	< .0001	100
Diabetes treated with Insulin	374 ± 8.0	312 ± 7.5	62 ± 12.1	0.0003	100
Liver disease	77 ± 1.6	69 ± 1.7	8 ± 1.6	0.8785	100
Cancer	225 ± 4.8	204 ± 4.9	21 ± 4.1	0.4318	100
Active endocarditis	238 ± 5.1	197 ± 4.7	41 ± 8.0	0.0014	100
Critical preoperative state	410 ± 8.7	300 ± 7.2	110 ± 21.4	< .0001	100
Preoperative ventilation	(exclusion)	(exclusion)	(exclusion)	(exclusion)	(exclusion)
Preoperative inotropic support	366 ± 7.8	266 ± 6.4	100 ± 19.5	< .0001	100
Cardiogenic shock	24 ± 0.5	18 ± 0.4	6 ± 1.2	0.0268	100
Intra-aortic balloon pump	58 ± 1.2	34 ± 0.8	24	< .0001	100
Hemoglobin, g/dl	13.5 ± 1.9	13.6 ± 1.9	12.6 ± 2.2	< .0001	99.7
Platelet count, K/ul	225 ± 69	225 ± 68	223 ± 77	0.6178	99.7
White blood cell count, K/ul	6.8 [5.7, 8.3]	6.8 [5.7, 8.2]	7.4 [6.0, 9.1]	< .0001	99.7
International normalized ratio	1.0 [1.0, 1.1]	1.0 [1.0, 1.0]	1.0 [1.0, 1.1]	< .0001	99.6
Preoperative SpO_2, %	97 [96, 98]	97 [96, 98]	97 [95, 98]	< .0001	100
Preoperative respiratory rate	16 [16, 18]	16 [16, 18]	16 [16, 18]	0.0015	97.0
Acuity				< .0001	100
Elective	3,740 ± 79.7	3,409 ± 81.5	331 ± 64.5		
Urgent	954 ± 20.3	772 ± 18.5	182 ± 35.5		
Surgical procedure type				< .0001	100
Aortic	100 ± 2.1	84 ± 2.0	16 ± 3.1		
Valve + Aortic	927 ± 19.8	807 ± 19.3	120 ± 23.4		
Valve + Aortic + CABG	84 ± 1.8	63 ± 1.5	21 ± 4.1		

(*Continued*)

Table 1. (Continued)

Characteristic	Entire Cohort N = 4694 n (%) or Mean ± SD/Median [Interquartile Range]	Postoperative Pulmonary Complication		*P* Value	% Cases with Complete Data
		No, N = 4181 (89.1%) n (%) or Mean ± SD/Median [Interquartile Range]	Yes, N = 513 (10.9%) n (%) or Mean ± SD/Median [Interquartile Range]		
Isolated CABG	969 ± 20.6	892 ± 21.3	77 ± 15.0		
Isolated Valve	2,078 ± 44.3	1,902 ± 45.5	176 ± 34.3		
Valve + CABG	536 ± 11.4	433 ± 10.4	103 ± 20.1		
Admission type				< .0001	100
Admit	3,488 ± 74.3	3,197 ± 76.5	291 ± 56.7		
Inpatient	1,206 ± 25.7	984 ± 23.5	222 ± 43.3		
Date of surgery by STS version				< .0001	100
2.52 (Jan 2006 through Dec 2007)	349 ± 7.4	312 ± 7.5	37 ± 7.2		
2.61 (Jan 2008 through June 2011)	1,286 ± 27.4	1,106 ± 26.5	180 ± 35.1		
2.73 (July 2011 through June 2014)	1,679 ± 35.8	1,482 ± 35.5	197 ± 38.4		
2.81 (July 2014 through May 2017)	1,380 ± 29.4	1,281 ± 30.6	99 ± 19.3		
ASA physical status				< .0001	100
III	1,476 ± 31.4	1,366 ± 32.7	110 ± 21.4		
IV	3,218 ± 68.6	2,815 ± 67.3	403 ± 78.6		
Intraoperative characteristics					
Perfusion time, h	2.2 ± 1.0	2.1 ± 1.0	2.9 ± 1.3	< .0001	100
Aortic crossclamp time, h	1.7 ± 0.8	1.7 ± 0.8	2.2 ± 1.1	< .0001	99.7
Anesthesia duration, h	6.5 [5.4, 7.9]	6.4 [5.3, 7.7]	7.7 [6.4, 9.4]	< .0001	100
Anesthesia provider¶				0.9443	100
Low LPV user	2,489 ± 53.0	2,214 ± 53.0	275 ± 53.6		
Medium LPV user	1,844 ± 39.3	1,646 ± 39.4	198 ± 38.6		
High LPV user	361 ± 7.7	321 ± 7.7	40 ± 7.8		
Intraoperative albuterol	57 ± 1.2	46 ± 1.1	11 ± 2.1	0.0416	100
Intraoperative diuretic‖	2,898 ± 61.7	2,588 ± 61.9	310 ± 60.4	0.5179	100
Intraoperative vasopressor infusion (phenylephrine, norepinephrine, vasopressin)	4,294 ± 91.5	3,815 ± 91.3	479 ± 93.4	0.1036	100
Intraoperative inotrope infusion (epinephrine, dobutamine, milrinone, isoproterenol, dopamine)	1,723 ± 36.7	1,397 ± 33.4	326 ± 63.6	< .0001	100
Total intraoperative opioid, oral morphine equivalents	300 [270, 360]	300 [270, 360]	300 [240, 375]	0.0177	99.9
Total intraoperative crystalloid, liter	3.0 [2.0, 4.3]	3.0 [2.0, 4.1]	3.4 [2.3, 5.3]	< .0001	98.8
Total intraoperative colloid, liter	0 [0, 0.5]	0 [0, 0.5]	0 [0, 0.5]	0.3498	100
Intraoperative packed red blood cells, units	0 [0,2]	0 [0, 2]	2 [0, 4]	< .0001	100
Intraoperative red blood cell salvage, liter	0 [0,0]	0 [0, 0]	0 [0, 0]	0.9154	100
Intraoperative fresh frozen plasma, units	0 [0,0]	0 [0, 0]	0 [0, 2]	< .0001	100
Intraoperative platelets, units	0 [0, 0]	0 [0, 0]	0 [0, 2]	< .0001	100
Intraoperative cryoprecipitate, units	0 [0, 0]	0 [0, 0]	0 [0, 0]	< .0001	100
Total urine output, liter	1.9 ± 1.2	1.9 ± 1.1	1.9 ± 1.4	0.4361	99.1
Pre-CPB ventilation/respiratory parameters					
Tidal volume, ml/kg predicted body weight	7.8 ± 1.5	7.8 ± 1.5	8.1 ± 1.7	0.0001	100
Peak inspiratory pressure, cm H_2O	17 [15, 20]	17 [15, 20]	19 [16, 22]	< .0001	100
Positive end-expiratory pressure, cm H_2O	5 [4, 5]	5 [4, 5]	5 [2, 5]	0.0359	100
Driving pressure, cm H_2O	13 [11, 16]	13 [11, 16]	15 [12, 18]	< .0001	100
SpO_2, %	99 [98, 100]	99 [98, 100]	99 [99, 100]	< .0001	100
Inspired FIO_2, %	97 [96, 98]	97 [95, 98]	97 [96, 98]	< .0001	100
Post-CPB ventilation/respiratory parameters					
Tidal volume, ml/kg predicted body weight	7.8 ± 1.5	7.7 ± 1.4	8.1 ± 1.6	< .0001	100
Peak inspiratory pressure, cm H_2O	18 [15, 20]	17 [15, 20]	20 [17, 23]	< .0001	100
Positive end-expiratory pressure, cm H_2O	5 [4, 5]	5 [4, 5]	5 [4, 5]	0.7216	100
Driving pressure, cm H_2O	13 [11, 16]	13 [11, 16]	16 [13, 19]	< .0001	100
SpO_2, %	100 [99, 100]	100 [99, 100]	100 [98, 100]	0.4913	100
Inspired FIO_2, %	97 [96, 98]	97.0 [96, 98]	97 [96, 98]	0.0033	100
Overall ventilation					
Bundled LPV strategy**	1,913 ± 40.8	1,787 ± 42.7	126 ± 24.6	< .0001	100

P value from independent *t* test, Mann–Whitney *U* test, or chi-square test, as appropriate.

*Defined by chronic lung disease at or above moderate *or* bronchodilator therapy within STS; or COPD at or above moderate on preoperative anesthesia history and physical. †Defined by functional capacity – Low (at or below four metabolic equivalents of task) on preoperative anesthesia history and physical. ‡Defined *via* STS as a history of any of the following: atrial fibrillation, atrial flutter, third degree heart block, ventricular fibrillation, or ventricular tachycardia. §Calculated using the Chronic Kidney Disease – Epidemiology Collaboration equation. ¶Defined as the frequency of primary anesthesiology attending using a bundled LPV strategy, as a proportion of all cardiac cases performed by the anesthesiology attending among the study population, transformed into tertiles. ‖Defined as intraoperative administration of furosemide, bumetanide, or mannitol. **Defined as intraoperative median values of tidal volume less than 8 ml/kg predicted body weight, positive end-expiratory pressure at or above 5 cm H_2O, and driving pressure less than 16 cm H_2O.

ASA, American Society of Anesthesiologists; CABG, coronary artery bypass graft; CPB, cardiopulmonary bypass; FIO_2, fraction of inspired oxygen; LPV, lung-protective ventilation; PA, pulmonary artery; SpO_2, oxygen saturation measured by pulse oximetry; STS, Society of Thoracic Surgeons.

the postoperative pulmonary complication primary outcome, we performed several sensitivity analyses, including an analysis of lung-protective ventilation separated into component parts: V_T below 8 ml/kg predicted body weight, driving pressure below 16 cm H_2O, or PEEP at or above 5 cm H_2O, and analysis of lung-protective ventilation strategies separately examined before and after CPB.

We also performed a sensitivity analysis, using a model that further restricted the number of covariates to the number of outcomes divided by 20.[45] Additionally, we compared our multivariable postoperative pulmonary complication model developed using least absolute shrinkage and selection operator for covariate selection with a multivariable postoperative pulmonary complication model including all noncollinear covariates with P less than 0.10. Finally, we performed subgroup analyses stratified by salient clinical characteristics.

Results

Of the 5,365 cardiac surgical cases reviewed, 4,694 met study inclusion criteria (fig. 1). Among these cases, 513 (10.9%) experienced a postoperative pulmonary complication. Individual nonmutually exclusive components of postoperative pulmonary complications included pneumonia (121 cases, 23.6% of postoperative pulmonary complications), prolonged ventilation longer than 24 h, (302, 58.9% of postoperative pulmonary complications), reintubation (115, 22.4% of postoperative pulmonary complications), and PaO_2/FIO_2 below 100 mmHg (164, 32.0% of postoperative pulmonary complications).

Patient Population – Baseline Characteristics and Univariate Analyses

As described in table 1, our study population had a median age of 62 yr, and 64% were men. Cardiac surgeries performed included coronary artery bypass grafting (20.6%), valve (44.3%), aorta (2.1%), and combination (33.0%). Cases were primarily elective (79.7%); remaining cases were urgent (20.3%). Our study population included cases across four time partitions by Society of Thoracic Surgeons Adult Cardiac Surgery Database version, including 349 (7.4%) from 1/1/2006 to 12/31/2007; 1,286 (27.4%) 1/1/2008 to 6/30/2011; 1,679 (35.8%) 7/1/2011 to 6/30/2014; 1,380 (29.4%) 7/1/2014 to 5/31/2017. An overall lung-protective ventilation strategy was used in 1,913 cases (40.8%); among components of a lung-protective ventilation strategy, a V_T below 8 ml/kg predicted body weight was achieved in 64% of cases, modified driving pressure below 16 cm H_2O in 71% of cases, and PEEP at or above 5 cm H_2O in 63% of cases. Adherence to varying thresholds and independent associations with postoperative pulmonary complications are provided in Supplemental Digital Content 1A through 1C (http://links.lww.com/ALN/C26). Crude incidence of postoperative pulmonary complications among cases using an overall lung-protective ventilation strategy was 6.6%, compared with 13.9% among cases without an overall lung-protective ventilation strategy (table 2). Postoperative pulmonary complications were associated with increased postoperative mortality as well as longer postoperative mechanical ventilation, ICU stay, and hospital stay (table 3). Patients receiving a lung-protective ventilation strategy were more commonly tall, nonobese, male, and nonsmokers (Supplemental Digital Content 2, http://links.lww.com/ALN/C27).

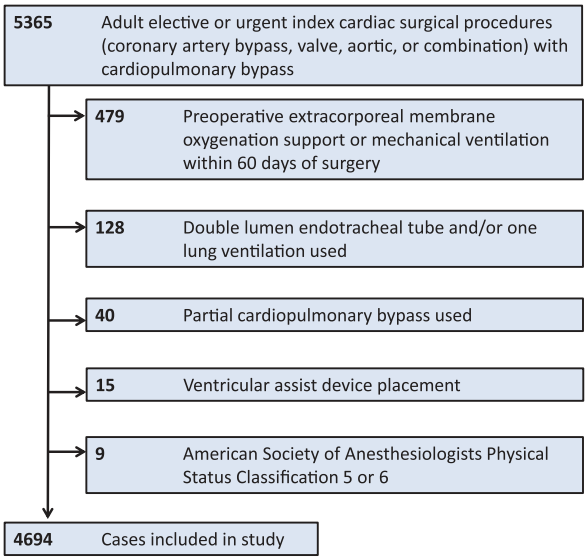

Fig. 1. Study inclusion and exclusion criteria.

Intraoperative Ventilator Management

Patients were ventilated with a cohort mean ± SD V_T of 7.8 ± 1.5 ml/kg predicted body weight, median (interquartile range) driving pressure of 13 (11 to 16) cm H_2O, and PEEP of 5 (4 to 5) cm H_2O. Compared with pre-CPB ventilator parameters, we observed no significant differences in post-CPB parameters (table 1). We observed distributions of overall per-case median ventilator parameters to be unimodal and rightward-skewed for V_T and driving pressure, *versus* a bimodal distribution (0 cm H_2O and 5 cm H_2O) for PEEP (fig. 2). Over the study period, we observed significant linear trends in ventilation practices: providers used decreasing V_T and driving pressure, and increasingly used PEEP ($P < 0.001$ for all trends; fig. 3).

Impact of Ventilator Parameters–Multivariable Analyses

Of the 4,694 cases studied, we observed data completeness rates greater than 99% for all but two risk adjustment variables, preoperative respiratory rate (97.0%) and total intraoperative crystalloid (98.8%). Peak inspiratory pressure and weight were removed from the model due to

Table 2. Summary of Primary Study Outcomes, Primary Outcome Components, and Bundled Lung-protective Ventilation Strategy

		Bundled LPV Strategy*		
	Entire Cohort N = 4694	No, 59.3% (n = 2781)	Yes, 40.7% (n = 1913)	*P* Value
Postoperative pulmonary complication	513 (10.9)	387 (13.9)	126 (6.6)	< .0001
Pneumonia	121 (2.6)	99 (3.6)	22 (1.2)	< .0001
Prolonged postoperative ventilation†	302 (6.4)	226 (8.1)	76 (4.0)	< .0001
Reintubation	115 (2.6)	85 (3.5)	30 (1.6)	< .0001
PaO_2/FIO_2 < 100 mmHg‡	164 (3.8)	131 (5.2)	33 (1.9)	< .0001

P value from independent *t* test or chi-square test, as appropriate.

*Defined as intraoperative median values of below 8 ml/kg predicted body weight, positive end-expiratory pressure at or above 5 cm H_2O, and driving pressure below 16 cm H_2O. †Defined as initial postoperative mechanical ventilation more than 24 h. ‡Within 48 h postoperatively while intubated.

FIO_2, fraction of inspired oxygen; LPV, lung-protective ventilation; PaO_2, arterial partial pressure of oxygen.

Table 3. Summary of Primary Study Outcomes, Secondary Study Outcomes, and Bundled Lung-protective Ventilation Strategy

		Postoperative Pulmonary Complication			Bundled LPV Strategy*		
	Entire Cohort N = 4,694	No, 89.1% (n = 4,181)	Yes, 10.9% (n = 513)	*P* Value	No, 59.3% (n = 2781)	Yes, 40.7% (n = 1913)	*P* Value
30-day postoperative mortality	49 (1.0)	19 (0.5)	30 (5.9)	< .0001	35 (1.3)	14 (0.7)	0.0810
Postoperative durations							
Total postoperative ventilator, h	17.2 (77.3)	7.1 (5.2)	99.4 (216.5)	< .0001	21.5 (96.1)	10.9 (34.3)	< .0001
Total ICU, h	73.9 (115.0)	57.6 (51.6)	207.1 (282.1)	< .0001	79.7 (137.6)	65.4 (69.3)	< .0001
Total hospital length of stay, days	7.5 (6.7)	6.5 (3.9)	15.7 (14.4)	< .0001	8.1 (7.8)	6.7 (4.4)	< .0001

P value from independent *t* test or chi-square test, as appropriate.

*Defined as intraoperative median values of below 8 ml/kg predicted body weight, positive end-expiratory pressure at or above 5 cm H_2O, and driving pressure below 16 cm H_2O.

ICU, intensive care unit; LPV, lung-protective ventilation.

multicollinearity (variance inflation factor greater than 10). Platelet count, international normalized ratio, total intraoperative opioid, preoperative respiratory rate, and history of cancer were removed, given a lack of use in previous validated cardiac surgery or postoperative pulmonary complication risk score models.[9,10,43] Multiple additional variables were removed via least absolute shrinkage and selection operator (denoted by "−" in Supplemental Digital Content 3, http://links.lww.com/ALN/C28). Through multivariable analyses adjusting for postoperative pulmonary complication risk factors, an intraoperative lung-protective ventilation bundle was independently associated with reduced postoperative pulmonary complications (adjusted odds ratio, 0.56; 95% CI, 0.42–0.75, figs. 4 and 5). Modelling lung-protective ventilation exposure as a treatment, we observed a number needed to expose of 18 (95% CI, 14–33) to prevent one postoperative pulmonary complication.

We observed no associations between a lung-protective ventilation bundle and minimum postoperative PaO_2/FIO_2 while intubated, initial postoperative ventilator duration in hours, length of ICU stay in hours, or length of hospital stay in days (Supplemental Digital Content 4, http://links.lww.com/ALN/C29). We observed similar findings for logarithmically transformed secondary outcomes. Postoperative mortality occurred in 49 cases (1.0%); our study was not adequately powered to analyze independent associations between lung-protective ventilation and mortality.

Among individual pulmonary complications (pneumonia, prolonged ventilation longer than 24 h, reintubation, and PaO_2/FIO_2 less than 100 mmHg postoperatively while intubated), a lung-protective ventilation bundle demonstrated univariate associations across all postoperative pulmonary complication components; after multivariable adjustment, a lung-protective ventilation bundle remained protective against all postoperative pulmonary complication components except for prolonged ventilation longer than 24 h (Supplemental Digital Content 5, http://links.lww.com/ALN/C30, and Supplemental Digital Content 6, http://links.lww.com/ALN/C31).

Sensitivity Analyses

When analyzing each component of the lung-protective ventilation bundle separately, we found that modified

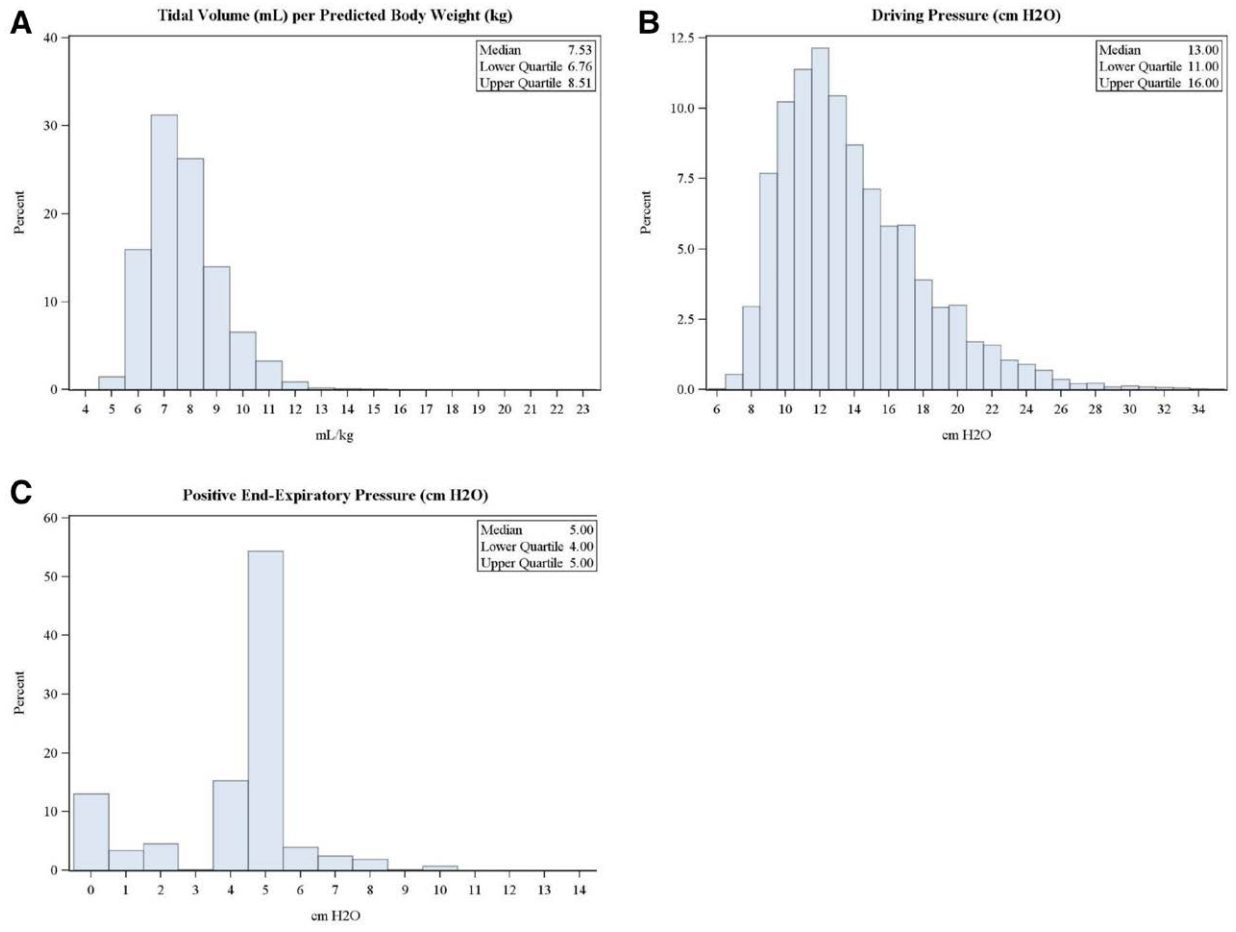

Fig. 2. Frequency distributions of per-case median intraoperative ventilator parameters, including tidal volume per predicted body weight, modified driving pressure, and positive end-expiratory pressure (in *A*, *B*, and *C*, respectively).

driving pressure driving pressure less than 16 cm H_2O was independently associated with reduced postoperative pulmonary complications (adjusted odds ratio, 0.51; 95% CI, 0.39–0.66) whereas V_T below 8 ml/kg predicted body weight and PEEP at or above 5 cm H_2O did not demonstrate significant independent associations (adjusted odds ratios [95% CIs] 0.99 [0.75–1.30] and 1.18 [0.91–1.53], respectively; fig. 4). Furthermore, driving pressure less than 16 cm H_2O was independently associated with improvements in all secondary outcomes.

When analyzing the lung-protective ventilation bundle as partitioned into pre-CPB and post-CPB periods, we observed no collinearity between corresponding pre-CPB and post-CPB variables (variance inflation factors below 10) and thus included all variables into a single model. We found that adherence to the post-CPB lung-protective ventilation bundle was associated with less postoperative pulmonary complications (adjusted odds ratio, 0.53; 95% CI, 0.38–0.74) whereas the pre-CPB lung-protective ventilation bundle was not associated with postoperative pulmonary complications (adjusted odds ratio, 1.19; 95% CI, 0.84–1.68, Supplemental Digital Content 7, http://links.lww.com/ALN/C32). Similarly, when analyzing the lung-protective ventilation components individually partitioned into pre-CPB and post-CPB periods, we observed no collinearity between corresponding pre-CPB and post-CPB components and thus included all variables into a single model. We observed post-CPB driving pressure less than 16 cm H_2O was associated with lesser likelihood of postoperative pulmonary complication (adjusted odds ratio, 0.57; 95% CI, 0.42–0.78), but neither the pre-CPB driving pressure below 16 cm H_2O (adjusted odds ratio, 0.77; 95% CI, 0.56–1.07) nor V_T below 8 ml/kg predicted body weight nor PEEP at or above 5 cm H_2O pre-CPB and post-CPB components was associated with postoperative pulmonary complications.

Logistic regression models using either least absolute shrinkage and selection of operator restricted to 24

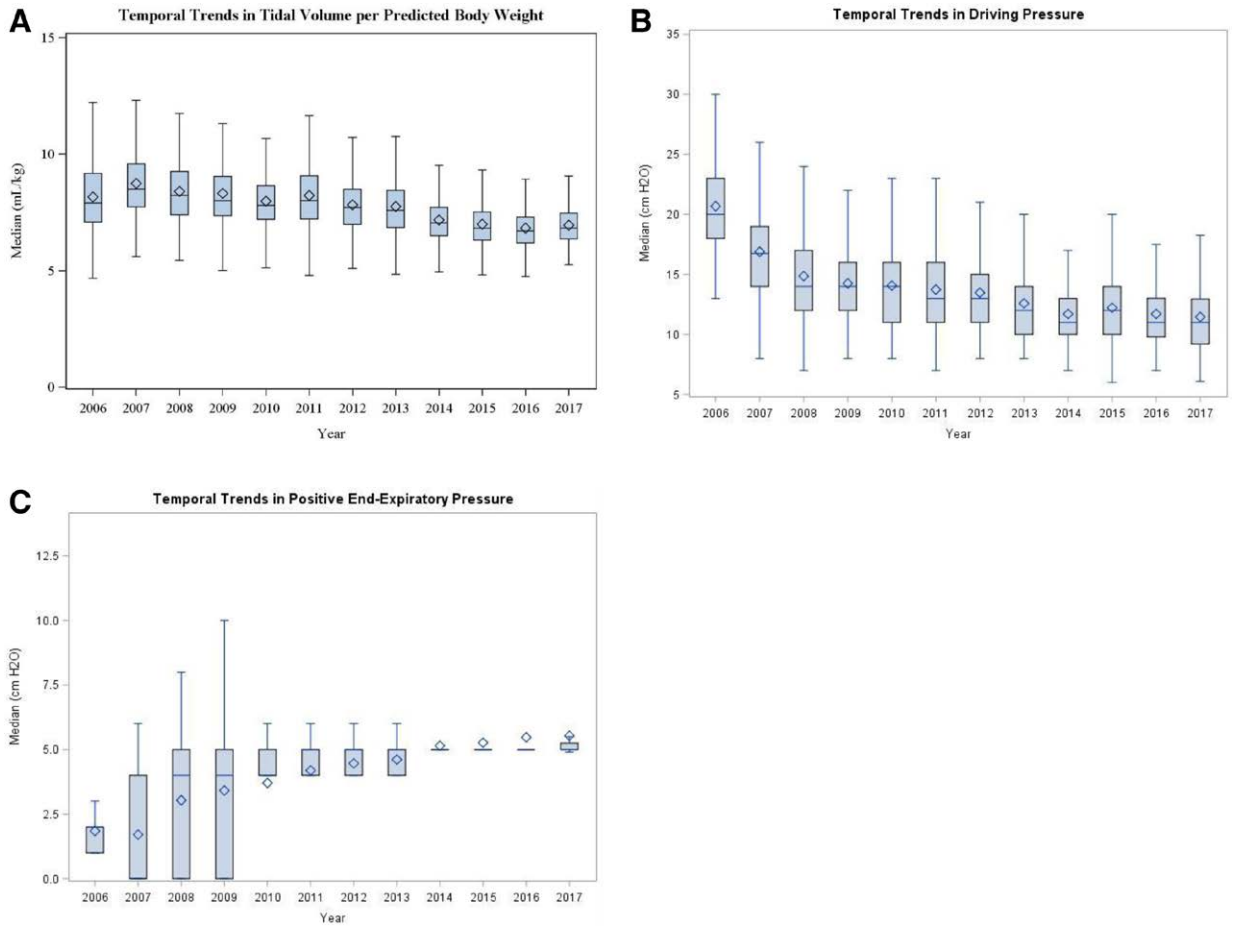

Fig. 3. Temporal trends in intraoperative ventilator strategies, including tidal volume per predicted body weight, modified driving pressure, and positive end-expiratory pressure (in *A*, *B*, and *C*, respectively).

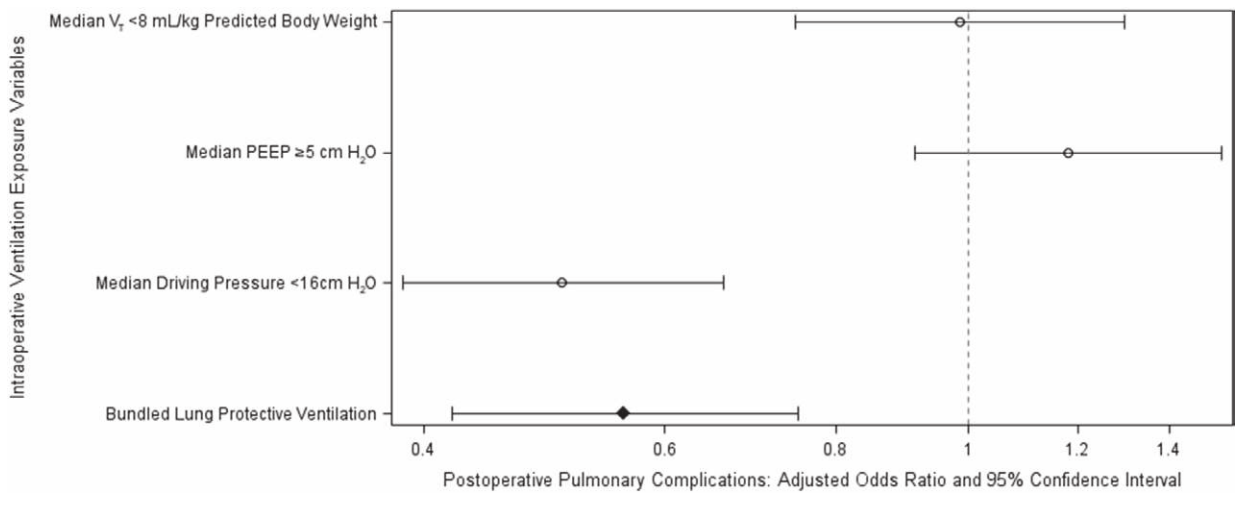

Fig. 4. Independent associations between intraoperative lung protective ventilation strategies and postoperative pulmonary complications.

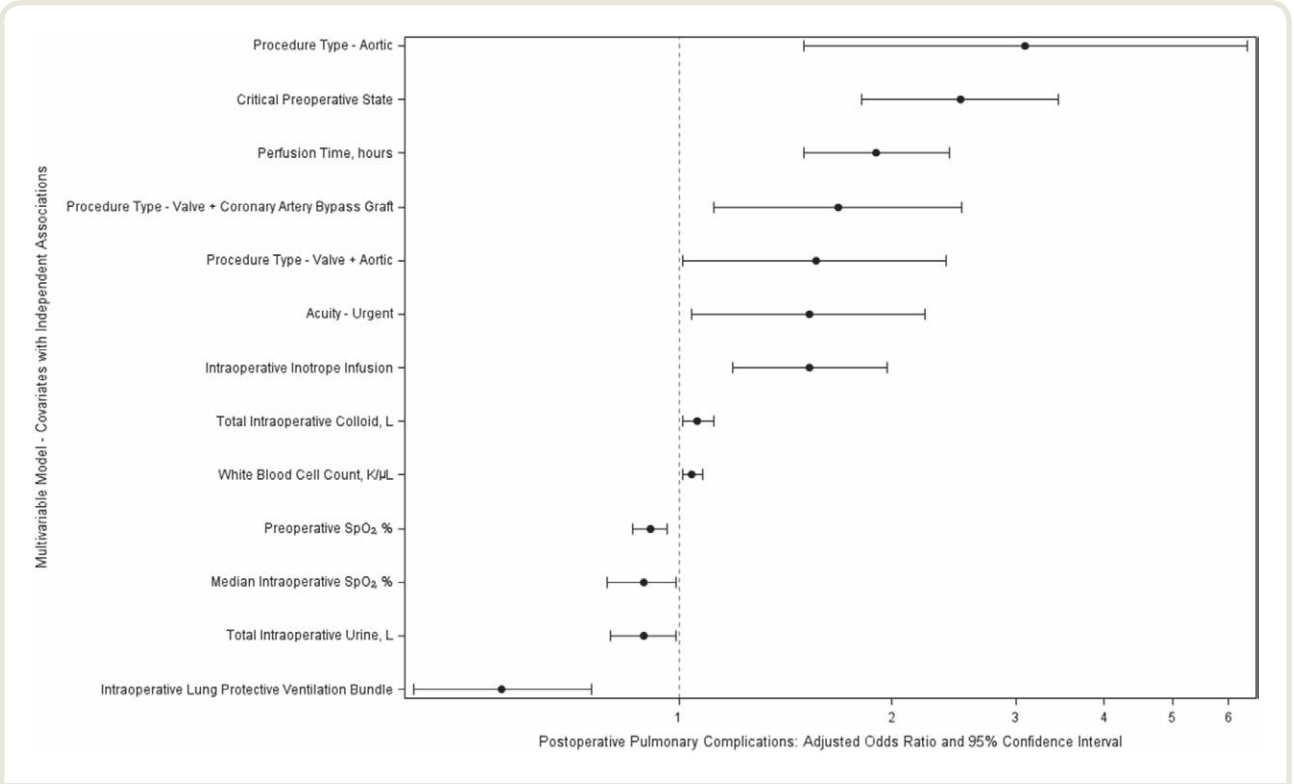

Fig. 5. Significant independent associations between multivariable model components and postoperative pulmonary complications.

covariates, or forward selection of univariate association thresholds ($P < 0.10$) found independent associations between lung-protective ventilation, driving pressure, and postoperative pulmonary complications, but not V_T or PEEP (Supplemental Digital Content 8, http://links.lww.com/ALN/C33, and Supplemental Digital Content 9, http://links.lww.com/ALN/C34). Finally, sensitivity analyses of clinically important subgroups yielded similar independent associations between the lung-protective ventilation bundle and outcomes. The protective association of the lung-protective ventilation bundle was observed in both males and females, in elective but not urgent cases, across all body mass index ranges, only in patients without chronic lung disease, and in patients undergoing valve procedures (Supplemental Digital Content 10, http://links.lww.com/ALN/C35).

Discussion

Using robust, validated observational databases, we report an overall pulmonary complication incidence of 10.9% after cardiac surgery, and identify an intraoperative lung-protective ventilation bundle as independently associated with a clinically and statistically significant reduction in pulmonary complications. Our study builds on existing literature by providing an analysis of the impact of intraoperative ventilation strategies on postoperative outcomes among a generalizable cardiac surgery population. Although unaccounted for in current risk scoring systems, we report that an intraoperative lung-protective ventilation strategy is independently associated with development of postoperative pulmonary complications. Through a sensitivity analysis evaluating components of the lung-protective ventilation bundle, we importantly note that driving pressure, but not V_T or PEEP, is independently associated with postoperative pulmonary complications.

Compared with previous literature, our findings demonstrate the importance of considering multiple components of lung-protective ventilation when evaluating the impact of mechanical ventilation on outcomes. Notably, we observed that not all components of lung-protective ventilation were independently associated with decreased postoperative pulmonary complications; however, a lung-protective ventilation bundled approach was independently associated with decreased postoperative pulmonary complications. Furthermore, within the lung-protective ventilation bundle studied, we observed driving pressure as the component primarily driving the association with reduced postoperative pulmonary complications, rather than V_T or PEEP. These findings offer insight toward sustaining a trend of expedited recovery from cardiac surgery, a process in which postoperative care teams are increasingly reliant on intraoperative practices—such as lung-protective ventilation—to target reduced postoperative complications and to safely enable rapid de-escalation of care on arrival to the ICU.[46,47]

Our study highlights the importance of driving pressure, and conversely the limitations of V_T and PEEP, as independently associated with postoperative pulmonary complications and secondary outcomes. We offer two hypotheses to explain these findings: (1) increased driving pressure is a marker for noncompliant lungs, assuming such patients are at increased risk of postoperative pulmonary complications and remain unidentified by model covariates; or (2) increased driving pressure reflects direct pulmonary injury via barotrauma as a postoperative pulmonary complication mechanism. Countervailing to a hypothesis that driving pressure serves as a marker for noncompliance, however, was our observation that lower V_T was not independently associated with increased postoperative pulmonary complications, as would be the case for increasingly noncompliant lungs at a given constant driving pressure exposure (controlled covariate). This finding was similarly observed in an analysis performed among 3,562 patients with acute respiratory distress syndrome enrolled across nine randomized trials.[17] Within a surgical population, a recent randomized, controlled trial demonstrated a driving pressure-guided ventilation strategy during one-lung ventilation to be similarly associated with a lower incidence of postoperative pulmonary complications compared with conventional ventilation strategies, during thoracic surgery.[48]

Additionally of note, in a sensitivity analysis analyzing pre-CPB driving pressure and post-CPB driving pressure separately, our observations that (1) pre-CPB and post-CPB variables were not collinear and (2) post-CPB driving pressure but not pre-CPB driving pressure below 16 cm H_2O was independently associated with postoperative pulmonary complications, suggests our driving pressure findings cannot solely be explained as a marker for poor baseline lung function. However, whether this independent association between post-CPB driving pressure below 16 cm H_2O and postoperative pulmonary complications can be explained by a direct lung injury hypothesis, *versus* a marker for varying degrees of CPB-induced pulmonary dysfunction, remains unanswerable based on our data. Other explanations for a lack of collinearity between pre-CPB and post-CPB driving pressure may include nuanced surgery stage-specific ventilation strategies, such as low V_T and low driving pressure during internal mammary artery surgical dissection and/or cannulation before CPB. Finally, although a driving pressure threshold below 16 cm H_2O enabled class balance between cases adherent *versus* nonadherent to an overall lung-protective ventilation bundle, an optimal driving pressure threshold defining lung-protective ventilation remains unclear, and likely varies by clinical context.

Our findings that lower intraoperative driving pressure was associated with improved outcomes suggest an opportunity for improved care through the implementation of an lung-protective ventilation protocol favoring lower driving pressure. Additionally, our observation that intraoperative driving pressure, but not V_T or PEEP, was independently associated with postoperative pulmonary complications, reflects a potential benefit of individualized ventilation strategies among patients with varying respiratory compliance (ignored with V_T-targeted ventilator management) or varying volume of aerated functional lung (ignored with uniform application of PEEP). However, given the observational nature of this study, our findings require prospective interventional evaluation and validation before large-scale adoption of the technique.

Our 10.9% observed incidence of postoperative pulmonary complications is consistent with previous studies.[1,6] However, this comparison is challenged by varied definitions of a postoperative pulmonary complication, which remain subject to debate. Our postoperative pulmonary complication definition is consistent with international consensus guidelines[35,36] and was derived from clinician-adjudicated data available within the Society of Thoracic Surgeons database or our electronic health record. Nonetheless, other recognized components of postoperative pulmonary complications include (1) atelectasis defined by radiographic evidence,[35] (2) pulmonary aspiration defined by clinical history and radiographic evidence,[35] (3) pleural effusion defined by radiographic evidence,[36] (4) pneumothorax,[35] (5) bronchospasm defined by expiratory wheezing treated with bronchodilators,[36] or (6) aspiration pneumonitis.[36] We determined *a priori* to exclude these additional postoperative pulmonary complication components in our composite outcome on the basis of either unclear clinical significance in a cardiac surgical population, underlying mechanisms likely not amenable to treatment via lung-protective ventilation, or lack of access to component-specific high-fidelity data across all patients in the study cohort.

Study Limitations

Our study has several limitations. First, we were unable to account for all potential mechanisms leading to a composite postoperative pulmonary complication. Mechanisms for pulmonary injury after cardiac surgery are multifactorial.[7] In our study, we investigated lung-protective ventilation as a means to reduce ventilator-induced lung injury, leading to postoperative pulmonary complications through mechanisms including volutrauma, barotrauma, and atelectasis, and respectively mitigated by lower V_T, lower driving pressure, and application of PEEP.[8] However, additional postoperative pulmonary complication mechanisms to be targeted by anesthesiologists include (1) pulmonary edema, mitigated by fluid and transfusion management,[49] (2) inadequate respiratory effort, mitigated by monitoring/reversal of neuromuscular blockade[50,51] or rapid-acting, opioid-limiting anesthetic agents,[52] and (3) respiratory infection, mitigated by ventilator associated pneumonia prevention bundles.[53,54] In our study, we successfully accounted for several of these targets as covariates. However, the relative importance of each technique, and the impact of lung-protective

ventilation on the association between such techniques and postoperative pulmonary complications, remains beyond the scope of this study.

In our study, precise times for sternotomy and chest closure were unavailable; however, cases excluded redo-sternotomies with protracted closed chest times. As such, driving pressures were assessed during open-chest conditions for a majority of intraoperative ventilation. Our study adds new data to studies of protective ventilation, previously performed during closed-chest conditions. As this relates to the driving pressures observed, our study may demonstrate comparatively less bias introduced by variable chest wall compliance. Thus, airway driving pressure in this study is likely to more closely reflect actual transpulmonary driving pressure, a determinant of dynamic lung strain.[55] Despite this strength, we caution generalizing our findings to more commonly studied patient populations ventilated under closed-chest conditions. We additionally caution generalizing our driving pressure threshold below 16 cm H_2O as lung-protective ventilation without consideration of clinical context. In previous studies of cardiac surgical populations,[16,37] thresholds for lung-protective ventilation defined by driving pressure (plateau pressure − PEEP) ranged from 8 to 19 cm H_2O. Such variation may be explained by (1) time of measurement (*e.g.*, intraoperative *versus* postoperative), (2) surgical conditions (*e.g.*, closed-chest *versus* open-chest), (3) patient populations and practice patterns varying by year and institution, and (4) covariates used for multivariable adjustment. However, it should be noted that despite such sources of variation influencing driving pressure-based lung-protective ventilation thresholds, independent associations between increased ventilator driving pressures and increased postoperative complications have been consistently observed.

Additional limitations to our study include those inherent to our single-center, observational study design: our conclusions require prospective multicenter validation. Patients receiving a lung-protective ventilation bundle were nonrandom; although multiple covariates associated with the lung-protective ventilation exposure were accounted for via multivariable analyses, unmeasured confounders influencing receiving a lung-protective ventilation bundle and impacting our postoperative pulmonary complication primary outcome was a source of potential bias. As pertaining to our lung-protective ventilation exposure variable, limitations included a lack of formal P_{plat} ventilator data for more accurate characterization of driving pressure. Although differences between ventilator peak inspiratory pressure and P_{plat} may be approximated in specified circumstances, the availability of all data necessary for calculations—and the degree to which confounding factors may bias such calculations (*e.g.*, patient differences in airway resistance, endotracheal tube obstructions from kinking/secretions, and the use of end-inspiratory pressure to approximate inspiratory pause pressure for calculating true P_{plat})—remain beyond the scope of our study.

Consistent with existing literature,[1,28] we represented the intraoperative period using lung-protective ventilation exposure median values—potentially failing to account for brief periods of profoundly injurious ventilation. Finally, although our study goal was to specifically examine relationships between intraoperative ventilation and postoperative pulmonary complications, relationships between postoperative ventilation and postoperative pulmonary complications were not studied.

Conclusions

Despite limitations, our study advances understanding of the relationship between intraoperative lung-protective ventilation and impact on costly, life-threatening postoperative pulmonary complication outcomes. In summary, we describe a 10.9% incidence of postoperative pulmonary complications among adults undergoing cardiac surgery. Importantly, we observed that a bundled lung-protective ventilation strategy was independently associated with a lower likelihood of postoperative pulmonary complications and that this was mostly associated with lower driving pressure. Through robust capture of variables describing intraoperative anesthesia management for cardiac surgery patients, our study provides data which may better inform postoperative pulmonary complication multivariable models in this population. Additionally, our findings offer targets for future prospective trials investigating the impact of specific lung-protective ventilation strategies for improving cardiac surgery outcomes.

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Competing Interests

The authors declare no competing interests beyond those described in the funding statement.

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Appendix 1. Postoperative Pulmonary Complications – Data Definitions

Postoperative Pulmonary Complication Component	Data Source	Definition
Prolonged initial postoperative ventilator duration longer than 24 h	STS database	Yes/No Indicate whether the patient had prolonged postoperative pulmonary ventilation longer than 24.0 h.
Pneumonia	STS database	Yes/No Indicate whether the patient had pneumonia according to the Centers for Disease Control and Prevention definition.
Reintubation	STS database	Yes/No Indicate whether the patient was reintubated during the hospital stay after the initial extubation. This may include patients who have been extubated in the OR and require intubation in the postoperative period.
Postoperative PaO_2:FIO_2 below 100 mmHg within 48 hours postoperatively while intubated	Hospital enterprise electronic health record (Epic Systems Corporation, USA)	Yes/No Indicate whether the patient had a postoperative PaO_2:FIO_2 below 100 mmHg within 48 h while intubated: • Intubated determined by ventilator mode • FIO_2 determined by ventilator setting • PaO_2 determined by arterial blood gas analysis

FIO_2, fraction of inspired oxygen; PaO_2, arterial partial pressure of oxygen; STS, Society of Thoracic Surgeons.

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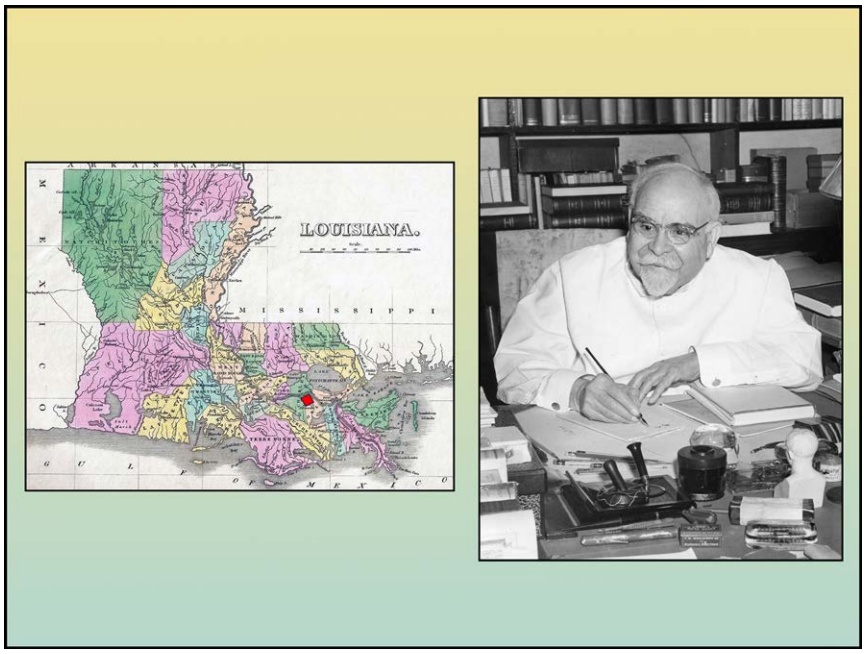
Dr. Rudolph Matas: Surgeon, Author, and an American Pioneer of Spinal Anesthesia



Born in Bonnet Carre, Louisiana (see *red diamond*, *left*), Rudolph Matas (1860 to 1957) was raised in Spain and then Texas before returning to his birth state for eventual medical schooling at the future Tulane University School of Medicine. After earning his M.D. at 19 yr of age, Dr. Matas began transforming himself into "the most learned surgeon" that Dr. Will Mayo had "ever known." Along the way, in 1889, Dr. Matas would also conduct America's first spinal anesthetic. By December of 1940, Matas was completing his eighth year of penning (*right*) a five-volume medical history of Louisiana. (Copyright © the American Society of Anesthesiologists' Wood Library-Museum of Anesthesiology.)

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