OBSERVATIONAL STUDY

OPEN

Hyperoxemia During Cardiac Surgery Is Associated With Postoperative Pulmonary Complications

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OBJECTIVES: The use of hyperoxemia during cardiac surgery remains controversial. We hypothesized that intraoperative hyperoxemia during cardiac surgery is associated with an increased risk of postoperative pulmonary complications.

DESIGN: Retrospective cohort study.

SETTING: We analyzed intraoperative data from five hospitals within the Multicenter Perioperative Outcomes Group between January 1, 2014, and December 31, 2019. We assessed intraoperative oxygenation of adult patients undergoing cardiac surgery with cardiopulmonary bypass (CPB). Hyperoxemia pre and post CPB was quantified as the area under the curve (AUC) of F_{IO_2} above 0.21 in minutes when the corresponding peripheral oxygen saturation was greater than 92% measured by pulse oximetry. We quantified hyperoxemia during CPB as the AUC of Pa_{O_2} greater than 200 mm Hg measured by arterial blood gas. We analyzed the association of hyperoxemia during all phases of cardiac surgery with the frequency of postoperative pulmonary complications within 30 days, including acute respiratory insufficiency or failure, acute respiratory distress syndrome, need for reintubation, and pneumonia.

PATIENTS: Twenty-one thousand six hundred thirty-two cardiac surgical patients.

INTERVENTIONS: None.

MEASUREMENTS AND MAIN RESULTS: During 21,632 distinct cardiac surgery cases, 96.4% of patients spent at least 1 minute in hyperoxemia (99.1% pre-CPB, 98.5% intra-CPB, and 96.4% post-CPB). Increasing exposure to hyperoxemia was associated with an increased risk of postoperative pulmonary complications throughout three distinct surgical periods. During CPB, increasing exposure to hyperoxemia was associated with an increased odds of developing postoperative pulmonary complications ($p < 0.001$) in a linear manner. Hyperoxemia before CPB ($p < 0.001$) and after CPB ($p = 0.02$) were associated with increased odds of developing postoperative pulmonary complications in a U-shaped relationship.

CONCLUSIONS: Hyperoxemia occurs almost universally during cardiac surgery. Exposure to hyperoxemia assessed continuously as an AUC during the intraoperative period, but particularly during CPB, was associated with an increased incidence of postoperative pulmonary complications.

KEY WORDS: cardiac surgery; hyperoxemia; postoperative pulmonary complications; supplemental oxygen

Postoperative pulmonary complications, including acute respiratory insufficiency or failure, pneumonia, and acute respiratory distress syndrome (ARDS), are significant causes of increased morbidity and mortality following cardiac surgery (1). Postoperative pulmonary complications are common following cardiac surgery, reported in approximately 25%

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KEY POINTS

Question: What is the association between intraoperative hyperoxemia during cardiac surgery with postoperative pulmonary complications?

Findings: Increasing exposure to hyperoxemia was associated with an increased risk of postoperative pulmonary complications throughout three distinct surgical periods. During cardiopulmonary bypass (CPB), increasing exposure to hyperoxemia was associated with an increased odds of developing postoperative pulmonary complications ($p < 0.001$) in a linear manner. Hyperoxemia before CPB ($p < 0.001$) and after CPB ($p = 0.02$) were associated with increased odds of developing postoperative pulmonary complications in a U-shaped relationship.

Conclusions: Exposure to hyperoxemia, assessed continuously during the intraoperative period, was associated with an increased incidence of postoperative pulmonary complications.

of patients (2–5). ARDS, the most severe pulmonary complication, occurs in up to 10% of patients following cardiac surgery (6, 7) and is associated with a 15–50% postoperative mortality (7). Therefore, an improved understanding of potential interventions to reduce postoperative pulmonary complications is critical to improving patient outcomes following cardiac surgery.

Hyperoxemia is commonly defined as Pao_2 greater than 100 mm Hg or saturation of oxygen (Spo_2) greater than 96% (8–11). However, specific criteria for hyperoxemia during cardiac surgery—particularly during cardiopulmonary bypass (CPB)—have not been established. We do know that excessive oxygenation is more common during CPB when compared with the pre- or post-CPB periods (12), and cardiac surgery patients are frequently oxygenated with a Fio_2 of 100% resulting in hyperoxemia (12, 13). Although potential benefits of hyperoxemia in cardiac surgery have been demonstrated (14, 15), an evolving body of literature suggests hyperoxemia has harmful consequences following cardiac surgery (2, 16, 17). Indeed, experts in the field of cardiac anesthesiology remain divided regarding the use of hyperoxemia during cardiac surgery (18–20). Since the lungs are minimally perfused during CPB, increased oxidative stress is likely the source of downstream lung injury (16). Persistent use of intraoperative hyperoxemia, despite potential harm, is multifactorial and likely due to clinician preferences, delay between exposure and pulmonary injury, and achieving an oxygenation "buffer" during transitions on/off CPB and from the operating room (OR) to ICU.

We sought to evaluate the impact of hyperoxemia during three distinct phases of cardiac surgery. The primary objective of this study was to investigate the relationship between hyperoxemia during cardiac surgery and postoperative pulmonary complications. We hypothesized that hyperoxemia during all phases of cardiac surgery is associated with an increased incidence of postoperative pulmonary complications.

MATERIALS AND METHODS

Study Design

Our multicenter observational study was approved by the Colorado Multiple Institutional Review Board (COMIRB no. 09-0674, November 13, 2019) and the Multicenter Perioperative Outcomes Group (MPOG), an extensive research and quality improvement consortium based at the University of Michigan. The MPOG database collects intraoperative anesthetic data from 51 academic and community hospitals in 21 states (21). We obtained waiver of informed consent for the use of deidentified data. All procedures were followed in accordance with the ethical standards of COMIRB and with the Helsinki Declaration of 1975. Methods for data collection, validation, mapping to universal concepts, and secure transfer of data have been previously described (22). The analytic plan was prespecified and approved by the MPOG Perioperative Clinical Research Committee. We conducted this study in accordance with the Reporting Studies Conducted Using Observational Routinely Collected Health Data statement, an extension of the Strengthening the Reporting of Observational Studies in Epidemiology reporting guidelines (**Supplemental Fig. 1,** http://links.lww.com/CCX/B154) (23, 24).

Study Population

Intraoperative records of patients greater than or equal to 18 years old who underwent cardiac surgery

with CPB between January 1, 2014, and December 31, 2019, were eligible for inclusion. January 1, 2014, was chosen to ensure electronic medical record compatibility across all eligible sites. We included patients with a case duration of at least 120 minutes, receiving general anesthesia with an endotracheal tube, CPB duration of at least one minute, and ASA physical status classification 1–4. We excluded patients who underwent emergency surgery, underwent circulatory arrest, or received either heart or lung transplantation (**Fig. 1**). After applying these criteria, we included only MPOG sites that were able to contribute more than 50 patients to the dataset, five of 51. We analyzed only the first surgical event for each patient encounter.

Exposure

We assessed intraoperative hyperoxemia before, during, and after CPB. CPB start and end were times derived from the anesthetic record. We collected FIO_2 from time of intubation to time of extubation or out of OR time (whichever was later). Hyperoxemia pre and post CPB was quantified as the per-minute area under the curve (AUC) of FIO_2 above 0.21 for minutes when the corresponding SpO_2 was greater than 92% and was normalized for procedure duration (13). In the case of missing FIO_2 data, FIO_2 values were carried forward for 5 minutes. If SpO_2 or FIO_2 were missing for longer than 5 minutes, we imputed the SpO_2 or FIO_2 values for the intervening minutes to be the mean of the bookending values. If there were no bookending SpO_2 or FIO_2 values within the surgical period (pre or post CPB), the data were considered missing. Missing data for either FIO_2 or SpO_2 made no contribution to the AUC. We normalized data separately for the pre- and post-CPB periods. Specifically, we divided the above-described AUC by the length of the corresponding procedural period. The length of the pre-CPB period was the number of minutes from anesthesia start to CPB start, and the length of the post-CPB period was the number of minutes from CPB end to anesthesia end. Frequency of observed, imputed, and missing values are described in **Supplemental Table 1** (http://links.lww.com/CCX/B154).

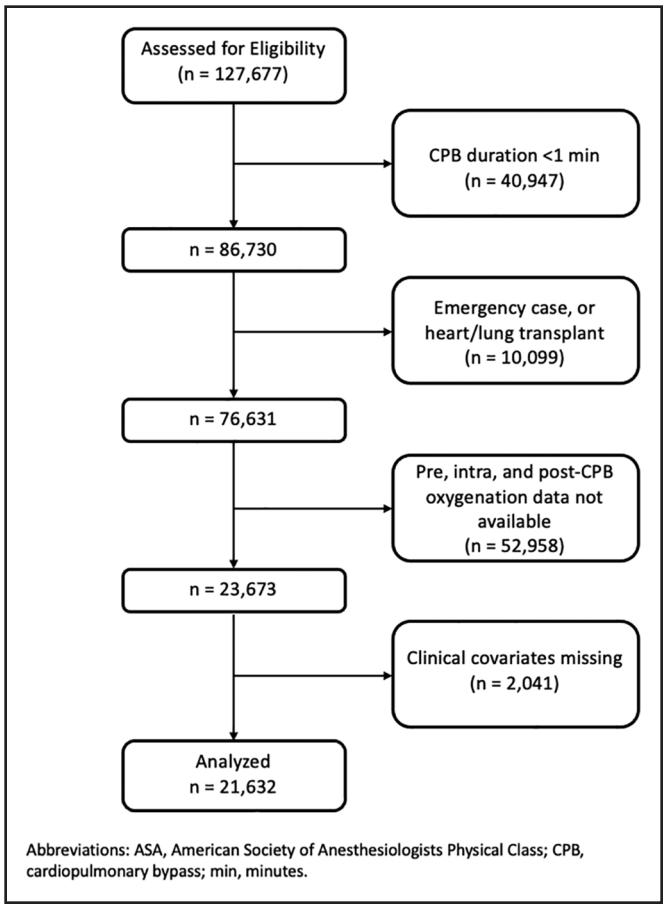

Figure 1. Consolidated Standards of Reporting Trials flow (CONSORT) diagram of exclusion criteria applied to the patient cohort. CPB = cardiopulmonary bypass.

During CPB, patient oxygenation occurs via a mechanical oxygenator, so FIO_2 is not a suitable measure of oxygen administration. Hyperoxemia during CPB was quantified as the AUC of PaO_2 greater than 200 mm Hg measured by arterial blood gas, normalized for duration of CPB. Since the threshold for hyperoxemia during CPB has not been well validated, we chose 200 mm Hg based on median PaO_2 targets during CPB as described by perfusionists (12). For minutes where PaO_2 measurements were missing, the value of PaO_2 for the intervening minutes was defined as the mean of the bookending values. For minutes prior to the first PaO_2 measurement but after CPB start, the value of PaO_2 was presumed to be equal to the first observed PaO_2 value. For minutes after the final PaO_2 measurement but prior to the end of CPB, the value of PaO_2 was imputed to be equal to the last observed PaO_2 value.

Outcomes

Our primary outcome was the incidence of postoperative pulmonary complications within 30 days of index hospitalization, defined via *International Classification of Diseases*, 9/10th revision (ICD 9/10)

codes. Postoperative pulmonary complications include acute respiratory insufficiency or failure, ARDS, need for reintubation, and pneumonia (25). We captured need for reintubation using the Current Procedural Terminology code 31500. If a subject did not have one of the relevant ICD 9/10 codes for postoperative pulmonary complications, they were classified as not experiencing a postoperative pulmonary complication. Secondary outcomes included in-hospital 28-day mortality, as reported by the American College of Surgeons National Surgical Quality Improvement Project.

Statistical Analysis

We considered the following covariates in our model: age, sex, body mass index, ASA class, chronic pulmonary disease, hypertension, circulation disorders, neurologic disorders, psychosis, alcohol abuse, drug abuse, and institution. All comorbidities were defined using the Elixhauser comorbidity index. We analyzed data from five institutions and excluded institutions with fewer than 50 observations from the final analytic dataset. Due to sparse missingness (< 8%) in the covariates of interest (Supplemental Table 1, http://links.lww.com/CCX/B154), we conducted a complete-case analysis with respect to hyperoxemia exposure and the covariates listed above.

We conducted a logistic regression analysis for postoperative pulmonary complications using the prespecified covariates and three hyperoxemia exposures (pre, during, and post CPB). We modeled three exposures jointly alongside clinical covariates, allowing us to determine the effect of hyperoxemia in each perioperative period conditional on the effect of hyperoxemia in the other two perioperative periods. We anticipated a potential "threshold" effect in the association of hyperoxemia exposure with postoperative pulmonary complications, whereby at a certain point, increasing exposure to hyperoxemia would sharply increase postoperative pulmonary complication risk. Thresholds were assessed via the "segmented" R package Version 1.3 (R Foundation for Statistical Computing, Vienna, Austria, 2022) in separate models for each of the three exposures. Although there was some evidence of a single threshold for the pre-CPB and post-CPB exposures (Davies test $p = 0.006$ and $p = 0.008$, respectively), the SEs for the estimated thresholds were large, thus precluding confident estimation of exact thresholds. Therefore, we flexibly modeled the effect of pre-CPB and post-CPB hyperoxemia using second-order polynomial terms. Orthogonal polynomials were generated via the R function poly. There was no evidence for a threshold effect or a polynomial effect in the association of intra-CPB hyperoxemia with postoperative pulmonary complications, and thus the untransformed intra-CPB exposure was included as a covariate with no higher order forms or transformations.

We assessed significance for the second-order polynomial form of the pre-CPB and post-CPB hyperoxemia exposures using a likelihood ratio test. Significance for the effect of intra-CPB hyperoxemia was assessed using a Wald test. All significance tests were assessed at a type I error rate of 5%. We employed partial dependence plots to visualize the relationship between pre-CPB and post-CPB hyperoxemia exposures and postoperative pulmonary complication risk. We generated partial dependence plots using the "pdp" R package Version 0.7. Confidence bounds for the partial dependence plots were estimated via nonparametric bootstrap with 500 resamples. All analyses in this study were performed using R Version 4.1.0 (R Foundation for Statistical Computing, Vienna, Austria, 2022) (26).

RESULTS

After applying relevant inclusion and exclusion criteria (Fig. 1), we analyzed 21,632 distinct patients from five sites undergoing cardiac surgery with CPB. The median age was 64 years, and 67.5% of included patients were male (**Table 1**). The vast majority of patients (99.3%) were classified as ASA physical class 3 or 4. Most patients had some form of preoperative cardiac or circulatory comorbidity (78% with hypertension, 58.6% with arrhythmias, and 76.7% with valvular heart disease), and 4,682 patients (21.6%) had chronic pulmonary disease (Table 1). The primary outcome, postoperative pulmonary complications within 30 days of the index procedure, occurred in 9,021 patients (41.7%). Patients who experienced postoperative pulmonary complications were older, more likely to have chronic cardiopulmonary comorbidities, and had greater 28-day mortality. We adjusted for these and other covariates in our final model. In-hospital mortality within 28 days of the index operation occurred in 290 patients (1.3%).

We stratified hyperoxemia exposure into three distinct time points: pre-CPB, intra-CPB, and post-CPB (**Fig. 2**). In the pre-CPB period, 99.1% of patients spent at least 1 minute in hyperoxemia. For the

TABLE 1.
Characteristics and Outcomes of Cardiac Surgical Patients

Characteristics, *n* (%)	PPCs, *N* = 9,021 (42%)	No PPCs[a], *N* = 12,611 (58%)
Demographics, *n* (%)		
Age, years; median (IQR)	65 (56–72)	64 (55–72)
Male sex	6,089 (67.5)	8,502 (67.4)
Body mass index, kg/m^2, median (IQR)	28.0 (24.7–32.1)	27.8 (24.6–31.8)
ASA class		
1	8 (0.1)	15 (0.1)
2	45 (0.5)	88 (0.7)
3	1,926 (21.4)	3,411 (27.0)
4	7,044 (78.1)	9,097 (72.1)
Congestive heart failure	4,077 (45.2)	4,689 (37.2)
History of cardiac arrhythmia	5,616 (62.3)	7,070 (56.1)
Valvular heart disease	6,780 (75.2)	9,808 (77.8)
Peripheral vascular disease	3,355 (37.2)	3,933 (31.2)
Hypertension	7,379 (81.8)	9,504 (75.4)
Chronic pulmonary disease	2,315 (25.7)	2,367 (18.8)
Neurologic disorders	838 (9.3)	633 (5.0)
Diabetes mellitus	2,218 (23.6)	2,158 (17.1)
Renal disease	2,386 (26.4)	2,245 (17.8)
Liver disease	657 (7.3)	463 (3.7)
Solid tumor without metastasis	217 (2.4)	225 (1.8)
Metastatic cancer	50 (0.6)	46 (0.4)
Coagulopathy	3,725 (41.3)	4,927 (39.1)
Obesity	1,748 (19.4)	2,383 (18.9)
Duration of cardiopulmonary bypass, min; median (IQR)	120 (86–169)	120 (86–166)
Procedure duration, min; median (IQR)	342 (279–435)	331 (266–412)
28-d mortality	224 (2.5)	66 (0.5)

IQR = interquartile range, PPCs = postoperative pulmonary complications.

[a]All baseline demographics were significantly different between the PPCs and no PPCs groups except for sex and presence of obesity.

intra-CBP and post-CPB periods, 98.5% and 96.4% of patients, respectively, spent at least 1 minute in hyperoxemia.

Increasing exposure to hyperoxemia assessed continuously as an AUC was associated with postoperative pulmonary complications in different ways between the three CBP periods (**Fig. 3**). In the pre-CPB period, exposure to hyperoxemia was associated with increased odds of developing postoperative pulmonary complications (p = 0.002) in a U-shaped relationship. Odds of postoperative pulmonary complications were greatest at both low (< second decile) and high (>fifth decile) exposures to hyperoxemia (**Fig. 3*A***). During CPB, increasing exposure to hyperoxemia was associated with an increased odds of developing postoperative pulmonary complications (p < 0.001) in a linear manner (**Fig. 3*B***). In the post-CPB period, exposure to hyperoxemia was also associated with the odds of developing postoperative pulmonary complications (p = 0.02) in a U-shaped relationship (**Fig. 3*C***). At the highest deciles of hyperoxemia exposure, the odds of developing postoperative pulmonary complications increase modestly during the post-CPB periods.

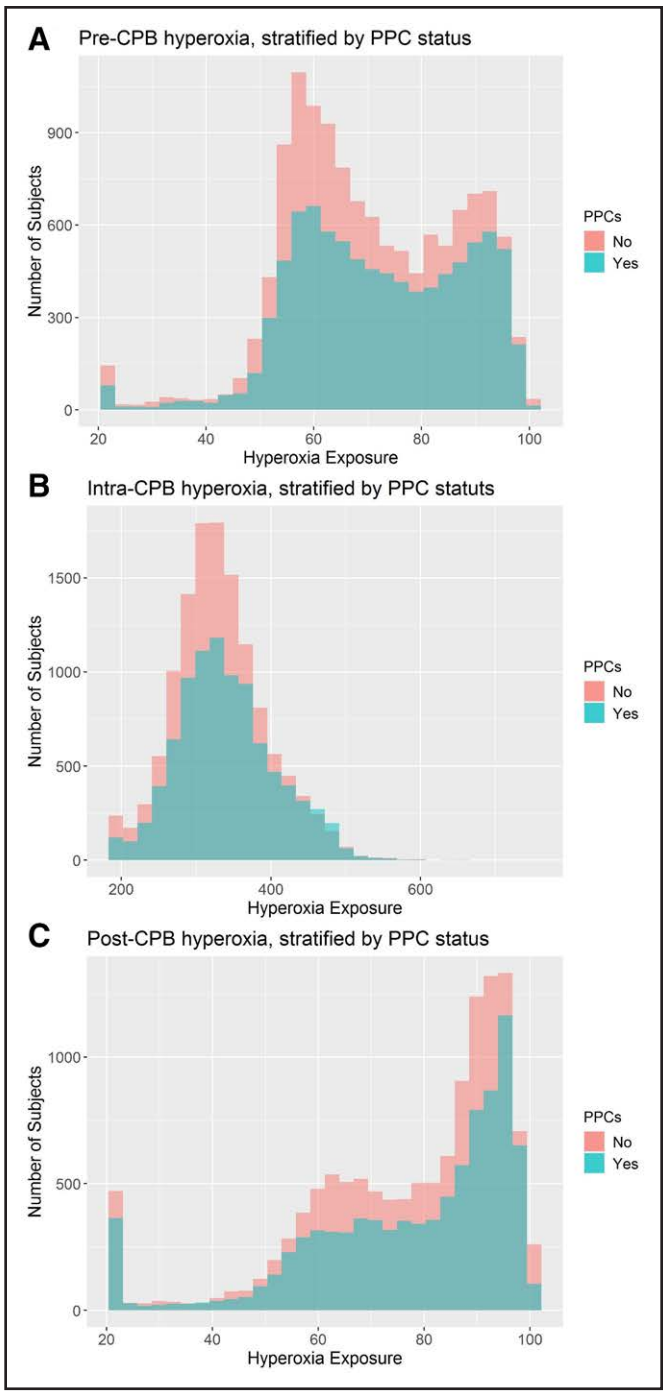

Figure 2. Distribution of hyperoxemia, stratified by postoperative pulmonary complications status displayed via overlaid histograms. **A**, Pre-cardiopulmonary bypass (CPB), **B**, intra-CBP, and **C**, post-CPB. For the pre- and post-CPB periods, median FIO_2 values are presented. For the intra-CPB period, median PaO_2 values are presented. PPC = postoperative pulmonary complication.

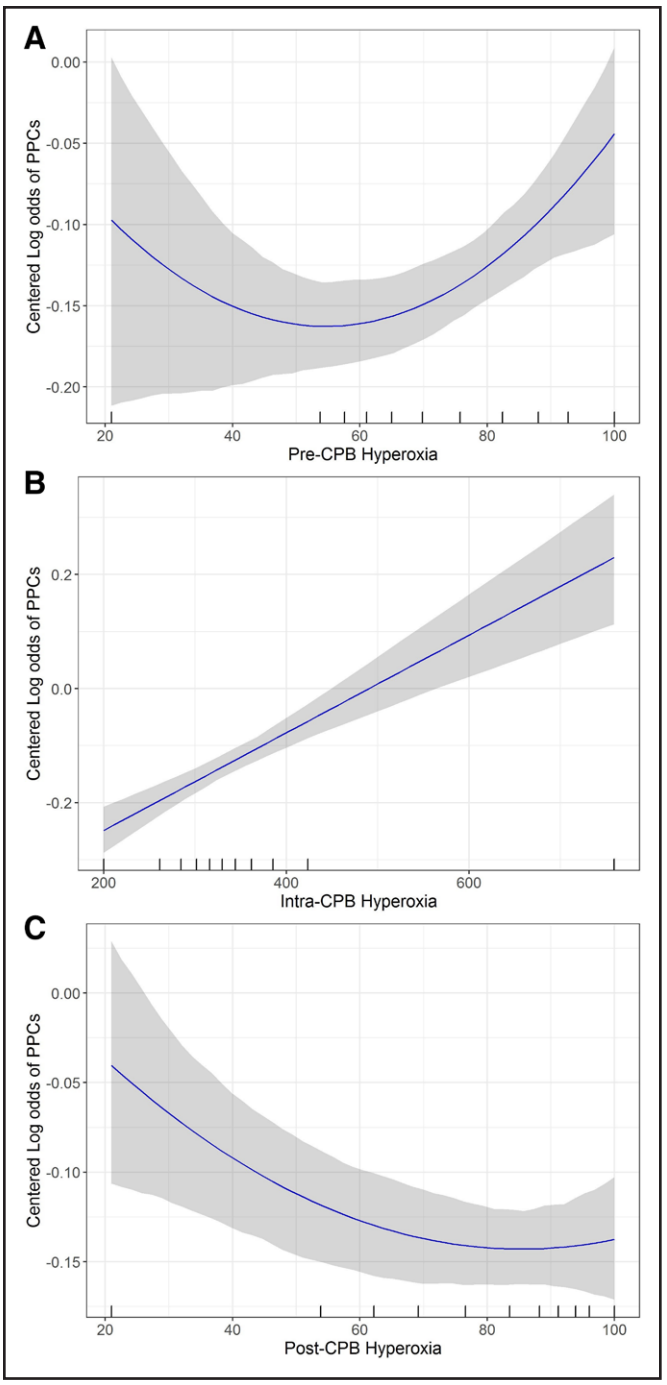

Figure 3. Association between hyperoxemia exposure and the adjusted log odds ratio of postoperative pulmonary complications at three time points as estimated via multiple logistic regression. The *x*-axes denote the mean FIO_2 for 2A/2C and the mean PaO_2 for 2B. *Tick marks* along the *x*-axes delineate the 10 deciles of distribution for hyperoxemia exposure, measured by area under the curve. Shaded regions represent the 95% bootstrap CI for the predicted log odds of postoperative pulmonary complications. **A**, Pre-cardiopulmonary bypass (CPB), **B**, intra-CPB, and **C**, post-CPB. PPC = postoperative pulmonary complication.

Pairwise comparisons of hyperoxemia and the adjusted odds of postoperative pulmonary complications are displayed in **Figure 4**. Hyperoxemia exposure in the post-CPB period is associated with decreased odds of developing postoperative pulmonary complications after accounting for the effect of pre-CPB hyperoxemia and intra-CPB hyperoxemia

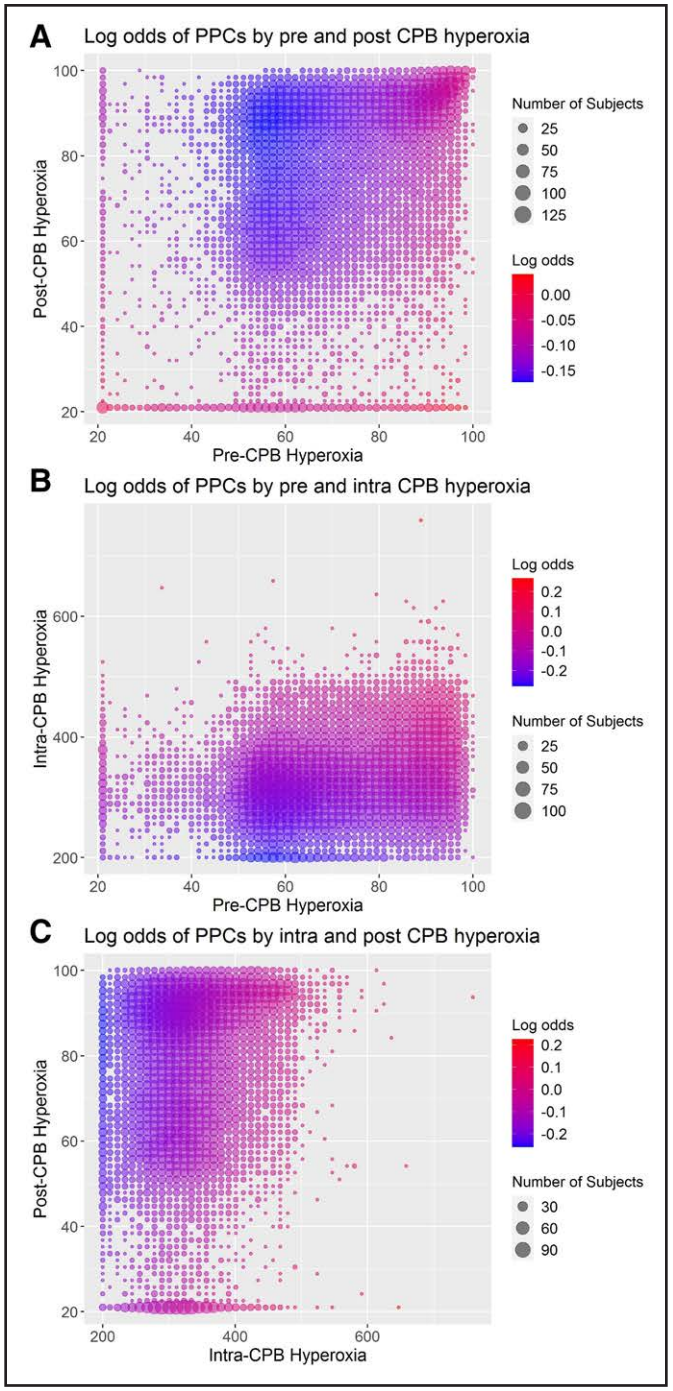

Figure 4. Association between pairwise combinations of hyperoxemia exposures and log odds ratio of postoperative pulmonary complications. Pairwise relationships between the hyperoxemia exposures and the adjusted log odds ratios of postoperative pulmonary complications (PPCs) were estimated via multiple logistic regression. The *size of each bubble* corresponds to the number of subjects who received each combination of hyperoxemia. *Bubble color* represents the log odds of postoperative pulmonary complications. The *color scale* is explained by the legend on the right of the plot. For pre- and post-cardiopulmonary bypass (CPB), *axes tick marks* indicate the median F_{IO_2} during the respective time period. For intra-CPB, *axes tick marks* indicate the median P_{aO_2} during the respective time period.

(**Fig. 4,** ***A*** and ***C***). Similarly, exposure during CPB is significantly associated with greater odds of developing postoperative pulmonary complications after accounting for the effects of pre-CPB hyperoxemia and post-CPB hyperoxemia (**Fig. 4,** ***B*** and ***C***). For all three comparisons, the odds of developing postoperative pulmonary complications were greatest at both extremes of hyperoxemia exposure. Increased time spent in hyperoxemia during CPB was associated with the greatest odds of developing postoperative pulmonary complications.

DISCUSSION

In this large multicenter cohort of patients undergoing cardiac surgery, hyperoxemia occurred more than 96% of the time before, during, and after CPB. Cumulative intraoperative exposure to hyperoxemia, assessed continuously as an AUC, was associated with the development of postoperative pulmonary complications in a linear relationship during CPB. Hyperoxemia was associated with postoperative pulmonary complications in a U-shaped relationship before and after CPB.

Hyperoxemia in the pre-CPB and post-CPB periods demonstrated a U-shaped association with postoperative pulmonary complications (Fig. 3, *A* and *C*). These figures imply that the extremes of hyperoxemia exposure are associated with postoperative pulmonary complication risk. However, the blue tick marks on the *x*-axis delineate the 10 deciles of hyperoxemia exposure. For example, prior to CPB (Fig. 3*A*), approximately 90% of subjects had a mean F_{IO_2}greater than53%. We, therefore, have little confidence in the values at the low end of hyperoxemia exposure, which contained only 10% of patient observations, and significantly greater confidence in those values greater than 53%, close to the nadir of the quadratic curve. This confidence is reflected by the width of the 95% bootstrap CI, which is narrower around the nadir of the curve and wider toward the extremes of the distribution. For nine of 10 deciles of patients, we observed a positive association between pre-CPB hyperoxemia and the odds of experiencing a postoperative pulmonary complication.

As shown in Figure 3*C*, the association between post-CPB hyperoxemia and odds of postoperative pulmonary complications (Fig. 3*C*) was more balanced. Approximately half of the observed patients experienced post-CPB hyperoxemia exposure less than the minimum point on the curve, whereas roughly half had

greater post-CPB hyperoxemia exposure. However, the slope of the curve after the minimum is low, whereas the slope of the curve prior to the minimum is steep. Therefore, for low levels of post-CPB hyperoxemia exposure, there is a strong negative relationship between hyperoxemia and postoperative pulmonary complication risk. Conversely, a strong positive relationship between post-CPB hyperoxemia exposure and odds of postoperative pulmonary complications does not exist at any exposure level. The association between hyperoxemia during CPB and odds of postoperative pulmonary complications demonstrated a positive linear relationship (Fig. 3*B*).

Our results are biologically plausible based on our current understanding of hyperoxemia-induced lung injury and clinical observations. Oxidative stress due to the production of reactive oxygen species (ROS) plays a key role in hyperoxemia-induced acute lung injury (27). Even brief exposure to hyperoxemia can increase ROS production (28). Exposure to ROS leads to altered surfactant composition, reduced mucociliary clearance, and histological damage resulting in atelectasis, reduced lung compliance, and increased risk of pulmonary infections (27). Indeed, arterial hyperoxemia has been associated with increased mortality in a variety of critically ill patient populations (29, 30).

Prior to CPB, Fio_2 is determined by the anesthesiology team. Short exposures to hyperoxemia during this period can induce acute lung injury. For example, if the Fio_2 is set to 100%, as it often is during cardiac surgery (13), ROS exposure quickly intensifies. Therefore, the association between increasing hyperoxemia exposure prior to CBP and postoperative pulmonary complications is plausible. During CPB, blood is oxygenated directly via the bypass circuit, directed by the perfusionist team. Hyperoxemia in this setting fuels neutrophil-related alveolar damage and oxygen-free radical formation. The linear relationship between hyperoxemia exposure and postoperative pulmonary complications we observed during CBP, therefore, aligns with the pathophysiology of hyperoxemia-induced lung injury. As oxygen delivery increases during CPB, the risk of direct pulmonary toxicity also increases. After separation from CPB, patients generally fall into one of two categories: patients with or without sufficient pulmonary function to achieve hyperoxemia. Those patients who were better able to achieve hyperoxemia likely had a greater cardiac output or at least improved cardiac and pulmonary function following CPB. Patients unable to achieve hyperoxemia may be struggling to maintain homeostasis, with multiple clinical derangements. Therefore, patients experiencing hyperoxemia during the post-CPB period may have better pulmonary function than the normoxemia group, which may explain why the association between hyperoxemia and postoperative pulmonary complications was less pronounced in the post-CPB period.

Although our findings indicate an association between hyperoxemia and postoperative pulmonary complications, the observational nature of our study precludes inferences of causation due to the potential for bias and unmeasured confounding. For example, postoperative pulmonary complications were more common in our cohort (42%) than previously reported following cardiac surgery (10–30%) (25, 31). This may be due to differences in documentation or billing practices between institutions. For example, some institutions encourage terms such as "acute hypoxemic respiratory failure" to denote people who remain intubated for any reason after surgery. However, such a diagnosis does not specifically equate to lung injury but rather indicates postoperative mechanical ventilation. Granular individual-level data were not available for every patient, and we encountered some data missingness (Supplemental Table 1, http://links.lww.com/CCX/B154). We corrected for data missingness by only analyzing patients and encounters for whom complete intraoperative oxygenation values and postoperative outcomes were available. We employed several assumptions in our cohort, including imputing Spo_2, Fio_2, and Pao_2 values. Additionally, we were unable to account for oxygenation during transport from OR to ICU when patients are frequently ventilated with 100% Fio_2 for a short period of time. Similarly, we were unable to capture the use of inhaled pulmonary vasodilators, such as nitric oxide, in the postoperative period. Pulmonary vasodilators often require invasive mechanical ventilation for administration. Next, it is possible that our definition of hyperoxemia during cardiac surgery is inaccurate. However, it has been validated by other established groups in cardiac surgery (13), and in the ICU (28). Transfusion of blood products was missing in 76.3% of patients in our cohort. Such transfusions may influence pulmonary outcomes by increasing the incidence of transfusion-related acute lung injury or transfusion-associated circulatory overload.

Unfortunately, given the high level of missingness in blood product transfusion data, we were unable to include this variable as a potential confounder for our primary outcome. Finally, oxygen delivery and target levels may vary based on altitude; one of our five sites is more than 5,403 feet above sea level (Aurora, CO). This correlates to a partial pressure of atmospheric oxygen ranging from approximately 130 mm Hg compared with 160 mm Hg at sea level (32). Therefore, our findings may not be generalizable to sea-level populations.

Prospective trials are necessary to determine the causal relationship between hyperoxemia during cardiac surgery and postoperative complications, including postoperative pulmonary complications. Identifying the Pao_2/Fio_2 level which is deemed "safe" during all periods of cardiac surgery represents one possible direction. One trial by Abou-Arab et al (33) randomized 440 patients to Fio_2 of 100% versus a goal Pao_2 less than 150 mm Hg during CPB. They found no difference in cardiovascular complications in the parent trial (33) or in neurologic/respiratory outcomes in a post hoc analysis (34). However, they only assessed hyperoxemia during CPB and not during the entire perioperative period. Another recent trial by Shaefi et al (35) randomized 100 patients to Pao_2greater than 70 mm Hg before and after CPB and a Pao_2 of 100–150 mm Hg during CBP versus maintaining a Fio_2 of 100% throughout the procedure. This group did not observe a difference in postoperative cognitive function between the oxygenation groups and noted that the optimal intraoperative oxygenation strategy during cardiac surgery remains uncertain. The forthcoming Risk of Oxygen during Cardiac Surgery trial (13) may reveal the optimal oxygenation targets for both cardiac anesthesiologists and perfusionists.

In conclusion, this large multicenter cohort study demonstrated that hyperoxemia occurs nearly all the time during cardiac surgery and is associated with the development of postoperative pulmonary complications in a dose-dependent fashion. Increasing exposure to hyperoxemia was associated with the development of postoperative pulmonary complications in a positive linear relationship during CPB and in a bimodal distribution before and after CPB. Prospective interventional studies are required to determine the causal association between hyperoxemia and clinical outcomes and assess optimal target oxygen concentrations in cardiac surgery patients.

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