Original Article

# Early Outcomes of a High $PaO_2/FiO_2$ Ratio during Cardiopulmonary Bypass

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## Abstract

***Background:*** *In cardiac surgery, supraphysiological oxygen levels are frequently applied perioperatively. In this study, we examined the postoperative effect of perioperative hyperoxemia in cardiac surgery.*

***Methods:*** *All patients who underwent mitral valve replacement via the standard sternotomy method between 2010 and 2021 were analyzed by scanning the hospital data system. The patients were divided into 2 groups: the hyperoxemic group (partial pressure of oxygen/fraction of inspired oxygen [$PaO_2/FiO_2$] >500 mmHg) (Group I) and the normoxemic group (300 mmHg < $PaO_2/FiO_2$ < 500 mmHg) (Group II) according to the mean of 3 $PaO_2/FiO_2$ values calculated by using 3 $PaO_2$ and 3 $FiO_2$ levels. Postoperative complications, the mechanical ventilation time, the need for noninvasive mechanical ventilator support, the length of intensive care unit (ICU) stay, the hospitalization period, and the mortality rate of the groups were compared.*

***Results:*** *A total of 78 patients were included in the study, and 53 of the patients (67.9%) were female. The mean age of the patients was 58.89±12.60 years. The total mechanical ventilation time was significantly higher in the hyperoxemic group than in Group II (P<0.001) (18.18±12.90 h and 11.45±7.85 h, respectively). The amount of postoperative bleeding was significantly higher in Group I (P=0.003) (539.47±201.74 mL and 417.50±186.93 mL, respectively). The total amount of blood products administered during surgery and ICU stay was higher in Group I (P=0.041) (3.55±1.59 units and 2.87±1.89 units, respectively).*

***Conclusion:*** *We observed that the group with hyperoxemia during cardiopulmonary bypass had a higher amount of postoperative bleeding and the need for transfusion, as well as a longer duration of mechanical ventilation and intensive care.*

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***Keywords:*** *Oxygen; Cardiopulmonary bypass; Morbidity; Mortality*

## Introduction

Although oxygen plays an important role in the synthesis of adenosine triphosphate, the energy source of cells, it also causes oxidation, which can lead to damage to the cells. This situation raises the paradox of oxygen toxicity.[1]

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While oxygen administration is a necessity in hypoxemia, there are concerns about the potentially harmful effects of excess oxygen administration such as absorption atelectasis, inflammatory cytokine release, central nervous system toxicity, and a decrease in cardiac output.[2, 3]

Thus far, supraphysiological levels of oxygen have been frequently administered in cardiac surgery patients perioperatively to protect against the non-physiological nature of the surgery and the risk of hypoxia induced by cardiopulmonary bypass (CPB), which can result in elevated levels of reactive oxygen species (ROS).[4, 5] High levels of ROS cause cellular damage and cardiac myocyte dysfunction, increased necrosis and apoptosis in myocytes, and vascular dysfunction. "Oxygen toxicity" caused by increased ROS formation can cause serious side effects, especially in ischemia/reperfusion situations such as in cardiovascular surgery.[6]

Despite technological advances in both surgical techniques and CPB equipment in cardiac surgery, mortality and morbidity remain high. It is common practice to deliver high levels of oxygen to the arterial blood, as blood gas sampling is usually done intermittently during the CPB procedure.[7] However, although the risks associated with hypoxemia are well known, the possible harmful effects of hyperoxemia are not fully considered.[8]

A partial pressure level of oxygen above 100 mmHg/13.3 kPa is defined as hyperoxemia.[9] In our study, we used the Horovitz index, which is more commonly used to evaluate pulmonary gas exchange. The normal value of this index is a partial pressure of oxygen/fraction of inspired oxygen ($PaO_2$/$FiO_2$) ratio exceeding 47 kPa (350 mmHg).[10] Although its definition is not completely clear, a $PaO_2/FiO_2$ value greater than 500 mmHg is considered hyperoxemia.[11]

In this study, we hypothesized that hyperoxemia would be associated with higher perioperative and postoperative mortality and morbidity, as well as longer mechanical ventilation (MV) and intensive care unit (ICU) stay.

## *Methods*

Our study was conducted at Istanbul University-Cerrahpaşa, Institute of Cardiology after the approval of the Istanbul University-Cerrahpaşa Clinical Research Ethics Committee (Date: 02.06.2021 Number: 103415). All patients who underwent mitral valve replacement via the standard sternotomy method between 2010 and2021 were analyzed by scanning the hospital data system.

The inclusion criteria consisted of age between 18 and 80 years, an ejection fraction (EF) of greater than 40%, undergoing elective conditions within the standard surgery period (> 6 h), and not experiencing any serious complications related to perioperative surgery or anesthesia. The exclusion criteria were composed of undergoing emergency surgeries, age over 80 years, an EF below 40%, undergoing additional surgical procedures (eg, aortic valve replacement, CPB graft surgery, and atrial septal defect closure), having pulmonary edema due to mitral or tricuspid insufficiency, having a history of chronic renal failure, having uncontrolled diabetes, having hypertension, suffering cerebrovascular events, experiencing serious surgical complications in the perioperative period, a surgical time longer than the standard surgery period (> 6 h) due to these complications, and death during the perioperative period.

The anesthesia procedure varied according to the preference of the anesthesiologist. Nonetheless, induction was started with an $FiO_2$ level of 0.8 in all the patients as this is the standard practice in our clinic. The $FiO_2$ level was reduced to 0.6 and ventilated with the pressure control mode such that the tidal volume was 6 to 8 mL/kg and the positive end-expiratory pressure (PEEP) was 3 to 5 cm/ $H_2O$. The standard sternotomy procedure was performed on all the patients. Heparin was administered at a dose of 3 to 4 mg/kg, with an activated clotting time (ACT) of over 400 seconds. CPB was started normothermically with 100% oxygen. Hypothermia was applied at 30 °C to 32 °C. The blood flow was adjusted at 2.4 L min-1 m2 according to the body surface, and the mean arterial pressure was kept between 60 and 80 mmHg. Blood cardioplegia was applied at 20-minute intervals in all the patients. Blood gas was taken after each cardioplegia. Blood transfusion (erythrocyte suspension) was applied to the patients whose hematocrit level was below 20% during CPB and below 28% after CPB. All the patients were taken to the ICU and connected to MV. The patients were followed up in the ICU for at least 36 hours.

The hospital database, anesthesia and perfusion observation forms, and patient files were examined. Additionally, the patients' demographic characteristics, previous diseases, preoperative echocardiographic values, blood gas values taken during the perioperative period, and inotropic agents administered after CPB were recorded.

The study population was divided into 2 groups: the hyperoxemic group ($PaO_2/FiO_2$>500 mmHg) (Group I) and the normoxemic group (300 mmHg<$PaO_2/FiO_2$<500 mmHg) (Group II) according to the mean of 3 $PaO_2/FiO_2$ values calculated by using the 3 $PaO_2$ values based on blood gas measurements obtained during CPB (at the beginning of CPB [$T_1$], during CPB [$T_2$], and at the termination of CPB [$T_3$]) and 3 $FiO_2$ levels. The EF (%) and pulmonary artery pressure (PAP) in the postoperative echocardiography results; postoperative complications including cerebrovascular events, infection, atrial fibrillation, and acute renal failure; the MV time; the need for noninvasive mechanical ventilator (NIMV) support, the length of ICU stay, the hospitalization period, and the mortality rate the groups were compared.

Statistical data analysis was performed using the IBM SPSS 21 Statistics (Armonk, NY). All the values are given as the mean with the standard deviation. The Kolmogorov–

Smirnov and Shapiro–Wilk tests were used to determine the distribution of the data set. Two independent groups were compared in the study. The Pearson $\chi^2$ and Fisher exact tests were employed to compare categorical data. The results of a multiple regression analysis, conducted to identify the possible confounding effects of age and sex, revealed that neither had any potentially confounding effects.[12] Comparison of quantitative variables between the 2 study groups was done using the Student *t* test and the Mann–Whitney *U* test. Mixed-design ANOVA was conducted to find statistical differences between the 2 groups in repeated measurements ($PaO_2$, $FiO_2$, mean arterial pressure [MAP], and lactate) at 3 time points. The Mauchly test of sphericity was used to test the sphericity assumption, and the test result was not significant. The sphericity assumption was met, and no correction was used. A P value of less than 0.05 was considered statistically significant.

## *Results*

Through scanning the hospital database, 114 patients who underwent isolated mitral valve replacement were identified out of 189 patients who underwent mitral valve replacement via the standard sternotomy method between 2010 and 2021. A total of 78 patients were included in the study. Fifty-three patients (67.9%) were female and 25 (32.1%) male. The mean age of the patients was 58.89±12.60 years. The mean cross-clamp time was 101.76±35.34 minutes, and the total CPB time was 156.78±58.66 minutes. The length of ICU stay of the patients was 4.19±4.62 days, and the hospitalization period was 7.41±3.16 days. While the total amount of bleeding in the first 24 hours postoperatively was 476.92±202.53 mL, the total amount of blood products (ie, red blood cells, fresh frozen plasma, and platelets) administered to the patients during the surgery and in the ICU was 3.21±1.77 units. A single inotropic agent was mostly used (48.7%) in case of a need for inotropic support after CPB. Dopamine, an inotropic agent, was used in all the patients (100%) at CPB termination. After CPB, 7.7% of the patients (n=6) needed a pacemaker, and 3.8% of these patients (n=3) needed a permanent pacemaker.

Moreover, 21.8% (n=17) of the patients required postoperative NIMV in the ICU. The mean duration of MV was 14.73±11.13 hours. In addition, 10.3% (n=8) of the patients were reintubated after extubation. Complications during the postoperative period are shown in Table 1. Six patients (7.7%) were readmitted to the ICU after being discharged from the ICU, and 8 patients (10.3%) died during the postoperative period.

The mean age was significantly higher in Group I (P=0.001). Measurement of the $PaO_2/FiO_2$ ratio at 3 different time points during CPB (ie, $T_1$, $T_2$, and $T_3$) was significantly higher in Group I (mean±SE=577.19±9.43, 95% CI: 558.39–595.98) than in Group II (mean±SE=455.57±9.20, 95% CI: 437.24–473.89) (Figure 1) ($F(2,152)=27.663$, $P<0.001$ $\eta^2_p=0.267$). There was no significant difference in terms of EF and PAP values in the preoperative period echocardiographic measurements between the groups (P=0.322 and P=0.202, respectively). No differences were noted between the groups concerning the total CPB and cross-clamp times (P=0.285 and P=0.478, respectively). The total MV time was

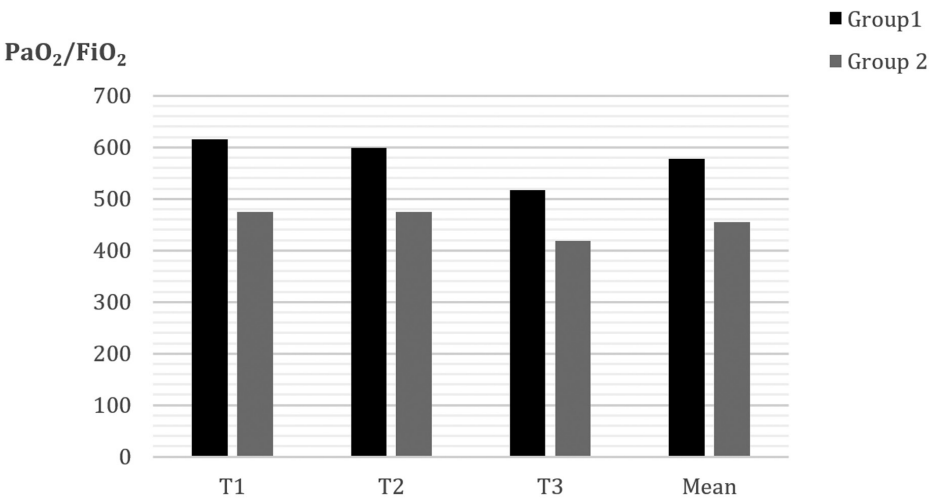


Figure 1. Variations of the $PaO_2/FiO_2$ ratio with time during cardiopulmonary bypass

Group 1: $PaO_2/FiO_2$>500 mmHg

Group 2: 300 mmHg<$PaO_2/FiO_2$<500 mmHg

$PaO_2$, Partial pressure of oxygen; $FiO_2$, Fraction of inspired oxygen; $T_1$, At the beginning of cardiopulmonary bypass; $T_2$, During cardiopulmonary bypass; $T_3$, At the termination of cardiopulmonary bypass

Table 1. Comparison of postoperative complications and measurements between the groups*

| | Group I ($PaO_2/FiO_2$>500 mmHg) (n=38) | Group II (300 mmHg<$PaO_2/FiO_2$<500 mmHg) (n=40) | P |
|---|---|---|---|
| Sex | | | 0.193 |
| Female | 29 (76.3) | 24 (60.0) | |
| Male | 9 (23.7) | 16 (40.0) | |
| Age (y) | 64.71±10.70 | 55.25±12.70 | 0.001 |
| Duration of CPB (min) | 169.61±74.88 | 144.58±34.06 | 0.285 |
| Cross-clamp duration (min) | 105.95±40.08 | 97.78±30.14 | 0.478 |
| Postoperative AF | 23 (60.5) | 18 (45.0) | 0.252 |
| Need for pacemakers | 5 (13.2) | 1 (2.5) | 0.104 |
| Need for permanent pacemakers | 2 (5.3) | 1 (2.5) | 0.610 |
| Postoperative PAP (mmHg) | 37.25±7.30 | 37.88±9.24 | 0.943 |
| Postoperative EF (%) | 58.55±4.64 | 57.75±7.42 | 0.993 |
| Total vasopressor requirement (NO) | | | 0.187 |
| 1 | 15 (39.5) | 23 (57.5) | |
| 2 | 14 (36.5) | 11 (27.5) | |
| 3 | 4 (10.5) | 5 (12.5) | |
| 4 | 5 (13.2) | 1 (2.5) | |
| Dopamine | 38 (100) | 40 (100) | n/a |
| Adrenaline | 21 (55.3) | 16 (40.0) | 0.262 |
| Noradrenaline | 7 (18.4) | 1 (2.5) | 0.027 |
| Dobutamine | 9 (23.9) | 7 (17.5) | 0.692 |
| Postoperative complications | | | |
| NIMV requirement | 8 (21.1) | 9 (22.5) | 1.000 |
| Duration of MV (h) | 18.18±12.90 | 11.45±7.85 | <0.001 |
| Reintubation | 3 (7.9) | 5 (12.5) | 0.712 |
| ARF | 7 (18.4) | 7 (17.5) | 1.000 |
| CVVHDF | 1 (2.6) | 1 (2.5) | 1.000 |
| CVE | 2 (5.3) | 1 (2.5) | 0.610 |
| Amount of bleeding (mL) | 539.47±201.74 | 417.50±186.93 | 0.003 |
| Transfusion (units) | 3.55±1.59 | 2.87±1.89 | 0.041 |
| SSI | 5 (13.2) | 6 (15) | 1.000 |
| Duration of ICU stay (d) | 4.68±4.69 | 3.73±4.55 | 0.082 |
| Duration of hospitalization (d) | 8.00±3.60 | 6.85±2.59 | 0.033 |
| Readmission to hospital | 3 (7.9) | 3 (7.5) | 1.000 |
| Mortality | 3 (7.9) | 5 (12.5) | 0.712 |
| Measurements taken during CPB | | | |
| $T_1$ $PaO_2$ (mmHg) | 306.03±42.51 | 260.75±55.40 | 0.001 |
| $T_1$ $FiO_2$ (%) | 0.51±0.09 | 0.55±0.09 | 0.038 |
| $T_1$ MAP (mmHg) | 68.13±7.02 | 66.73±6.45 | 0.359 |
| $T_1$ lactate (mmol/L) | 1.02±0.30 | 1.24±0.71 | 0.349 |
| $T_2$ $PaO_2$ (mmHg) | 265.92±26.67 | 235.03±36.09 | <0.001 |
| $T_2$ $FiO_2$ (%) | 0.45±0.05 | 0.50±0.05 | <0.001 |
| $T_2$ MAP (mmHg) | 72.53±7.60 | 73.33±7.38 | 0.718 |
| $T_2$ lactate (mmol/L) | 1.10±0.38 | 1.43±0.76 | 0.042 |
| $T_3$ $PaO_2$ (mmHg) | 252.82±42.40 | 239.3±35.70 | 0.131 |
| $T_3$ $FiO_2$ (%) | 0.50±0.10 | 0.58±0.10 | 0.001 |
| $T_3$ MAP (mmHg) | 72.58±7.88 | 74.15±7.21 | 0.312 |
| $T_3$ lactate (mmol/L) | 1.22±0.39 | 1.75±0.99 | 0.015 |
| $T_1$ $PaO_2/FiO_2$ (mm/Hg) | 615.35±91.77 | 474.52±77.18 | <0.001 |
| $T_2$ $PaO_2/FiO_2$ (mm/Hg) | 599.04±68.06 | 474.10±58.90 | <0.001 |
| $T_3$ $PaO_2/FiO_2$ (mm/Hg) | 517.16±112.98 | 418.09±75.10 | <0.001 |
| Mean $PO_2/FiO_2$ (mm/Hg) | 577.18±75.72 | 455.47±34.02 | <0.001 |

*Data are presented as mean±SD or n (%).

CPB, Cardiopulmonary bypass; AF, Atrial fibrillation; PAP, Pulmonary artery pressure; EF, Ejection fraction; NIMV, Noninvasive mechanical ventilator; MV, Mechanical ventilation; ARF, Acute renal failure; CVVHDF, Continuous venovenous hemodiafiltration; CVE, Cerebrovascular event; SSI, Surgical site infection; ICU, Intensive care unit; $PaO_2$, Partial pressure of oxygen; $FiO_2$, Fraction of inspired oxygen; MAP, Mean arterial pressure; $T_1$, At the beginning of cardiopulmonary bypass; $T_2$, During cardiopulmonary bypass; $T_3$, At the termination of cardiopulmonary bypass

significantly higher in the hyperoxemic group than in Group II (P<0.001). The amount of postoperative bleeding was significantly higher in Group I (P=0.003) (539.47±201.74 mL and 417.50±186.93 mL, respectively). The total amount of blood products administered during surgery and the ICU length of stay were higher in Group I (3.55±1.59 units and 2.87±1.89 units, respectively; P=0.041). While the length of stay in the ICU was similar when the 2 groups were compared (P=0.082), the total length of hospital stay was significantly higher in Group I (8.00±3.60 d and 6.85±2.59 d, respectively; P=0.033). No significant difference was found in the mortality rate between the groups (P=0.712) (Table 1).

EF and PAP measurements during the postoperative period were similar in both groups (P=0.993 and P=0.943, respectively). The lactate value measured at 3 different time points increased significantly more in Group II than in Group I (P<0.001).

## Discussion

The current study is one of the rare cardiac surgery studies with a methodology in which perioperative hyperoxemia was defined using the $PaO_2/FiO_2$ ratio. In this retrospective study, hyperoxemia during CPB in mitral valve repair had negative effects on morbidity. In addition, we observed that hyperoxemia during CPB increased the amount of postoperative bleeding and blood transfusion requirement. Although the length of ICU stay was not affected, the duration of MV was prolonged in hyperoxemic patients, and the total length of hospital stay increased. However, the mortality rate did not differ between the groups.

Pulmonary toxicity due to hyperoxemia was initially described by Smith.[13] In addition to the direct toxic effect of oxygen on the lungs due to elevated ROS, increased alveolar oxygen concentrations also lead to absorption atelectasis. Non-ventilated but perfused areas of the lung increase the intrapulmonary shunt and decrease the arterial oxygen fraction. Hypoxic pulmonary vasoconstriction is a physiological response against increased intrapulmonary shunts, but it is inhibited by elevated oxygen levels. For the mitigation of this situation, high postoperative oxygen administration constantly leads to elevated absorption atelectasis conditions, resulting in a vicious circle.

Prolonged MV duration is one of the most important complications of cardiac surgery.[14] Various strategies have been performed to shorten the duration of MV, including the performance of reaching a low tidal volume and trying new ventilator modes.[15] It was observed that liberal oxygen therapy ($PO_2$=190–300 mmHg) was associated with prolonged MV duration compared with conservative oxygen therapy ($PO_2$=75–112 mmHg).[16] In a more recent study, Jakutis et al16 showed that the duration of MV was longer in patients with severe hyperoxemia ($PO_2$>300 mmHg) during CPB. Various studies have also indicated that hypoxemia affects the duration of MV in cardiac surgery.[7, 17, 18] As a significant result, in our study, we found that the duration of MV was longer in hyperoxemic patients.

It is noteworthy that various studies have reported different values of hyperoxemia. Different studies have used $PaO_2$, $FiO_2$, or $FiO_2/PO_2$, similar to our study. In addition to these different values, the baseline values were also different. The $FiO_2$ and $PaO_2$ values that should be used during the perioperative or postoperative period in CPB have not been fully clarified, except for a study that recommended keeping $FiO_2$ at 35% during CPB.[19]

The World Health Organization (WHO) in 2016 recommended high $FiO_2$ (80%) for 2 to 6 hours during the peri- and postoperative periods to prevent surgical site infection (SSI). However, the results of studies on this subject are contradictory.[20] Although several studies have shown that high oxygen prevents SSI, larger studies have shown that there is no association between high oxygen levels and SSI.[16, 21-23] In a study by Pryor et al[24] on general surgery patients, it was shown that the use of high perioperative $FiO_2$ did not reduce the overall incidence of SSI, but it could have harmful effects (bleeding and increased need for transfusion). In this study, no positive effect of hyperoxemia on SSI was observed.

Hyperlactatemia has been widely accepted as a marker of tissue hypoxia/hypoperfusion. It is thought that hyperlactatemia may result not only from tissue hypoxia or anaerobic glycolysis but also from increased or accelerated aerobic glycolysis while responding to stress conditions.[25] In a study on female runners, it was observed that hyperoxemia decreased lactate levels. Sevuk et al[26] reported lower lactate levels in patients with hyperoxemia during CPB and suggested that it could be used to prevent tissue hypoxia. Similarly, in our study, lactate levels of hyperoxemic patients during CPB were lower than those of Group II.

Hyperoxemia causes a direct vasoconstrictive effect and increases coronary vascular resistance, as well as systemic vascular resistance.[27] It also leads to the deterioration of diastolic dysfunction by altering the calcium balance of myocytes.[28, 29] These conditions may lead to the deterioration of coronary and systemic perfusion during cardiac surgery. Studies on patients with cardiac disease have reported that those with hyperoxemia have higher cardiac enzymes than normoxemic patients.[30, 31] Although cardiac enzymes were not measured in our study, similar results were observed in both groups in terms of EF and PAP measured during the pre- and postoperative periods to evaluate cardiac function. In addition, the higher requirement for noradrenaline and pacemakers at the end of CPB in the hyperoxemic group in our study can be considered an indicator of myocardial dysfunction.

Cardiac ICUs are special units that provide care to patients after cardiac surgery or those who are critically ill. The

maintenance provided in these units requires a great deal of effort and cost. Therefore, both short ICU stays (<24 h) and early discharges (<5 d) are recommended after cardiac surgery.[32] In a study by Sutton et al[33] conducted on cardiac surgery patients, an increase in both ICU and hospital stays was observed in hyperoxemic patients. Similar to our study, in a study by Jakutis et al,[16] while the duration of ICU stay was not affected by hyperoxemia, the length of hospital stay was prolonged. In our study, the length of stay in the ICU was not affected despite the prolongation of the MV period with the routine postoperative ICU stay of at least 36 hours in the cardiac surgery protocols applied in our clinic.

Studies in the literature regarding the effect of hyperoxemia on bleeding and transfusion need are limited. Hyperoxemia is also associated with alterations in blood flow, capillary damage, intravascular hemolysis, and platelet dysfunction.[34] In our study, consistent with a study by Belbour et al, more postoperative bleeding and need for transfusion were observed in hyperoxemic patients. Both the amount of bleeding and the increase in the need for transfusion were the factors that significantly affected morbidity and mortality in cardiac surgery patients. Nonetheless, more studies are required to evaluate the relationship between hyperoxemia and the amount of bleeding.

Cardiac surgery is a type of surgery with a high mortality rate compared with many other surgical fields. Whereas there are studies showing that hyperoxemia increases mortality, several other studies have reported that it has no effect.[35-38] In our study, the mortality rates of hyperoxemic and normoxemic patients were similar.

Although our study was retrospective and the number of patients was relatively small, uncomplicated isolated mitral valve patients selected for the study represent a very specific group with many exclusion criteria. Sex (men) and age (older) are among the most important non-modifiable risk factors for coronary artery diseases.[39] Moreover, women carry a higher risk of events and mortality after CPB at a young age.[40] As a limitation of our study, the patients in Group I were older than those in Group II. Still, the large number of women in Group I may clear up the confusion.

## Conclusion

The results of the present study showed that the group with hyperoxemia during cardiopulmonary bypass had a higher amount of postoperative bleeding and the need for transfusion. In addition, the duration of mechanical ventilation and ICU stay was longer. Hyperoxemia, which is almost routinely applied to prevent hypoxia in cardiac surgery, may increase postoperative morbidity. Therefore, conservative oxygen treatments may be preferred in cardiac surgery protocols, especially during cardiopulmonary bypass.

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## References

1. Martin DS, McKenna HT, Morkane CM. Intraoperative hyperoxemia: an unnecessary evil? Anesth Analg 2016;123:1643.
2. Chu DK, Kim LH, Young PJ, Zamiri N, Almenawer SA, Jaeschke R, Szczeklik W, Schünemann HJ, Neary JD, Alhazzani W. Mortality and morbidity in acutely ill adults treated with liberal versus conservative oxygen therapy (IOTA): a systematic review and meta-analysis. Lancet 2018;391:1693-1705.
3. Rodríguez-González R, Martín-Barrasa JL, Ramos-Nuez Á, Cañas-Pedrosa AM, Martínez-Saavedra MT, García-Bello MÁ, López-Aguilar J, Baluja A, Álvarez J, Slutsky AS, Villar J. Multiple system organ response induced by hyperoxia in a clinically relevant animal model of sepsis. Shock 2014;42:148-153.
4. Heinrichs J, Lodewyks C, Neilson C, Abou-Setta A, Grocott HP. The impact of hyperoxia on outcomes after cardiac surgery: a systematic review and narrative synthesis. Can J Anaesth 2018;65:923-935.
5. Shaefi S, Marcantonio ER, Mueller A, Banner-Goodspeed V, Robson SC, Spear K, Otterbein LE, O'Gara BP, Talmor DS, Subramaniam B. Intraoperative oxygen concentration and neurocognition after cardiac surgery: study protocol for a randomized controlled trial. Trials 2017;18:600.
6. Young RW. Hyperoxia: a review of the risks and benefits in adult cardiac surgery. J Extra Corpor Technol 2012;44:241-249.
7. McGuinness SP, Parke RL, Drummond K, Willcox T, Bailey M, Kruger C, Baker M, Cowdrey KA, Gilder E, McCarthy L, Painter T; SO-COOL investigators. A multicenter, randomized, controlled phase IIb trial of avoidance of hyperoxemia during cardiopulmonary bypass. Anesthesiology 2016;125:465-473.
8. Duclos G, Rivory A, Rességuier N, Hammad E, Vigne C, Meresse Z, Pastène B, D'journo XB, Jaber S, Zieleskiewicz L, Leone M. Effect of early hyperoxemia on the outcome in severe blunt chest trauma: a propensity score-based analysis of a single-center retrospective cohort. J Crit Care 2021;63:179-186.
9. Reidy BTG, Whyte P, Neligan PJ. Is oxygen toxic? In: Deutschman CS, Neligan PJ, eds. Evidence-Based Practice of Critical Care. 3rd ed. Philadelphia: Elsevier; 2020. p. 36-42.
10. Horovitz JH, Carrico CJ, Shires GT. Pulmonary response to major injury. Arch Surg 1974;108:349-355.
11. Karbing DS, Kjaergaard S, Smith BW, Espersen K, Allerød C, Andreassen S, Rees SE. Variation in the $PaO_2/FiO_2$ ratio with $FiO_2$: mathematical and experimental description, and clinical relevance. Crit Care 2007;11:R118.
12. Pourhoseingholi MA, Baghestani AR, Vahedi M. How to control confounding effects by statistical analysis. Gastroenterol Hepatol Bed Bench 2012;5:79-83.
13. Smith JL. The pathological effects due to increase of oxygen tension in the air breathed. J Physiol 1899;24:19-35.
14. Crawford TC, Magruder JT, Grimm JC, Kemp CD, Suarez-Pierre A, Zehr KJ, Mandal K, Whitman GJ, Conte JV, Higgins RS, Cameron DE, Sciortino CM. The paradoxical relationship between donor distance and survival after heart transplantation. Ann Thorac Surg 2017;103:1384-1391.
15. Eisner MD, Thompson T, Hudson LD, Luce JM, Hayden D, Schoenfeld D, Matthay MA; Acute Respiratory Distress Syndrome Network. Efficacy of low tidal volume ventilation in patients with different clinical risk factors for acute lung injury and the acute respiratory distress syndrome. Am J Respir Crit Care Med

2001;164:231-236.
16. Jakutis G, Norkienė I, Ringaitienė D, Jovaiša T. Severity of hyperoxia as a risk factor in patients undergoing on-pump cardiac surgery. Acta Med Litu 2017;24:153-158.
17. Lee JS, Kim JC, Chung JY, Hong SW, Choi KH, Kwak YL. Effect of arterial oxygen tension during reperfusion on myocardial recovery in patients undergoing valvular heart surgery. Korean J Anesthesiol 2010;58:122-128.
18. Smit B, Smulders YM, de Waard MC, Boer C, Vonk AB, Veerhoek D, Kamminga S, de Grooth HJ, García-Vallejo JJ, Musters RJ, Girbes AR, Oudemans-van Straaten HM, Spoelstra-de Man AM. Moderate hyperoxic versus near-physiological oxygen targets during and after coronary artery bypass surgery: a randomised controlled trial. Crit Care 2016;20:55.
19. Toraman F, Evrenkaya S, Senay S, Karabulut H, Alhan C. Adjusting oxygen fraction to avoid hyperoxemia during cardiopulmonary bypass. Asian Cardiovasc Thorac Ann 2007;15:303-306.
20. Wenk M, Van Aken H, Zarbock A. The new World Health Organization recommendations on perioperative administration of oxygen to prevent surgical site infections: a dangerous reductionist approach? Anesth Analg 2017;125:682-687.
21. Greif R, Akça O, Horn EP, Kurz A, Sessler DI; Outcomes Research Group. Supplemental perioperative oxygen to reduce the incidence of surgical-wound infection. N Engl J Med 2000;342:161-167.
22. Schietroma M, Cecilia EM, Carlei F, Sista F, De Santis G, Piccione F, Amicucci G. Prevention of anastomotic leakage after total gastrectomy with perioperative supplemental oxygen administration: a prospective randomized, double-blind, controlled, single-center trial. Ann Surg Oncol 2013;20:1584-1590.
23. Stall A, Paryavi E, Gupta R, Zadnik M, Hui E, O'Toole RV. Perioperative supplemental oxygen to reduce surgical site infection after open fixation of high-risk fractures: a randomized controlled pilot trial. J Trauma Acute Care Surg 2013;75:657-663.
24. Pryor KO, Fahey TJ, 3rd, Lien CA, Goldstein PA. Surgical site infection and the routine use of perioperative hyperoxia in a general surgical population: a randomized controlled trial. JAMA 2004;291:79-87.
25. Garcia-Alvarez M, Marik P, Bellomo R. Stress hyperlactataemia: present understanding and controversy. Lancet Diabetes Endocrinol 2014;2:339-347.
26. Sevuk U, Altindag R, Baysal E, Yaylak B, Adiyaman MS, Akkaya S, Ay N, Alp V. The effects of hyperoxaemia on tissue oxygenation in patients with a nadir haematocrit lower than 20% during cardiopulmonary bypass. Perfusion 2016;31:232-239.
27. Thomson AJ, Drummond GB, Waring WS, Webb DJ, Maxwell SR. Effects of short-term isocapnic hyperoxia and hypoxia on cardiovascular function. J Appl Physiol (1985) 2006;101:809-816.
28. Mak S, Azevedo ER, Liu PP, Newton GE. Effect of hyperoxia on left ventricular function and filling pressures in patients with and without congestive heart failure. Chest 2001;120:467-473.
29. Guensch DP, Fischer K, Yamaji K, Luescher S, Ueki Y, Jung B, Erdoes G, Gräni C, von Tengg-Kobligk H, Räber L, Eberle B. Effect of hyperoxia on myocardial oxygenation and function in patients with stable multivessel coronary artery disease. J Am Heart Assoc 2020;9:e014739.
30. Stub D, Smith K, Bernard S, Nehme Z, Stephenson M, Bray JE, Cameron P, Barger B, Ellims AH, Taylor AJ, Meredith IT, Kaye DM; AVOID Investigators. Air versus oxygen in ST-segment-elevation myocardial infarction. Circulation 2015;131:2143-2150.
31. Inoue T, Ku K, Kaneda T, Zang Z, Otaki M, Oku H. Cardioprotective effects of lowering oxygen tension after aortic unclamping on cardiopulmonary bypass during coronary artery bypass grafting. Circ J 2002;66:718-722.
32. Peterson ED, Coombs LP, Ferguson TB, Shroyer AL, DeLong ER, Grover FL, Edwards FH. Hospital variability in length of stay after coronary artery bypass surgery: results from the Society of Thoracic Surgeon's National Cardiac Database. Ann Thorac Surg 2002;74:464-473.
33. Sutton AD, Bailey M, Bellomo R, Eastwood GM, Pilcher DV. The association between early arterial oxygenation in the ICU and mortality following cardiac surgery. Anaesth Intensive Care 2014;42:730-735.
34. Joachimsson PO, Sjöberg F, Forsman M, Johansson M, Ahn HC, Rutberg H. Adverse effects of hyperoxemia during cardiopulmonary bypass. J Thorac Cardiovasc Surg 1996;112:812-819.
35. Halter M, Jouffroy R, Saade A, Philippe P, Carli P, Vivien B. Association between hyperoxemia and mortality in patients treated by eCPR after out-of-hospital cardiac arrest. Am J Emerg Med 2020;38:900-905.
36. de Jonge E, Peelen L, Keijzers PJ, Joore H, de Lange D, van der Voort PH, Bosman RJ, de Waal RA, Wesselink R, de Keizer NF. Association between administered oxygen, arterial partial oxygen pressure and mortality in mechanically ventilated intensive care unit patients. Crit Care 2008;12:R156.
37. Eastwood G, Bellomo R, Bailey M, Taori G, Pilcher D, Young P, Beasley R. Arterial oxygen tension and mortality in mechanically ventilated patients. Intensive Care Med 2012;38:91-98.
38. Page D, Ablordeppey E, Wessman BT, Mohr NM, Trzeciak S, Kollef MH, Roberts BW, Fuller BM. Emergency department hyperoxia is associated with increased mortality in mechanically ventilated patients: a cohort study. Crit Care 2018;22:9.
39. Sattartabar B, Ajam A, Pashang M, Jalali A, Sadeghian S, Mortazavi H, Mansourian S, Bagheri J, Karimi AA, Hosseini K. Sex and age difference in risk factor distribution, trend, and long-term outcome of patients undergoing isolated coronary artery bypass graft surgery. BMC Cardiovasc Disord 2021;21:460.
40. Hosseini K, Yavari N, Pashang M, Jalali A, Nalini M, Majdi Nassab F, Sadeghian S, Salehi Omran A, Bagheri J, Poorhosseini H, Salarifar M, Ahmadi Tafti SH, Tajdini M. Sex difference in the risk factor distributions and outcomes after coronary artery bypass graft surgery in the young population. Eur J Cardiothorac Surg 2022;62:ezab475.