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Association Between Early Postoperative Fraction of Inspired Oxygen and Pulmonary Complications After Coronary Artery Bypass Grafting: A Retrospective Cohort Study Using Public Databases

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Abstract

Background

Patients undergoing coronary artery bypass grafting (CABG) frequently require postoperative mechanical ventilation and oxygen therapy. However, whether higher early postoperative fraction of inspired oxygen (FiO_2) exposure is associated with an increased risk of postoperative pulmonary complications (PPCs) remains uncertain. This study evaluated the association between early postoperative FiO_2 exposure and PPCs after CABG using the MIMIC-IV database and externally validated the findings in the eICU database.

Methods

We conducted a retrospective cohort study using MIMIC-IV version 3.1 as the derivation cohort and the eICU Collaborative Research Database as the external validation cohort. The MIMIC-IV cohort included 5,457 postoperative CABG patients, and the eICU validation cohort included 4,521 patients. Early postoperative FiO_2 exposure was defined as the mean FiO_2 during the first 6 h after ICU admission and was categorized as ≤ 0.60, 0.61–0.80, and > 0.80. The primary outcome was a composite of PPCs, including prolonged mechanical ventilation, reintubation, and pneumonia. Multivariable logistic regression, continuous exposure analysis per 0.1 increase in FiO_2, restricted cubic spline (RCS) analysis, propensity score weighting, and subgroup analyses were performed.

Results

In the MIMIC-IV cohort, the incidence of PPCs increased across FiO_2 categories: 5.51% (45/817) in the ≤ 0.60 group, 8.10% (261/3,223) in the 0.61–0.80 group, and 14.61% (207/1,417) in the > 0.80 group ($P < 0.001$). In the eICU cohort, the corresponding rates were 9.41% (320/3,400), 14.25% (113/793), and 26.52% (87/328), respectively ($P < 0.001$). In fully adjusted logistic regression, FiO_2 >0.80 remained associated with higher odds of PPCs in MIMIC-IV (OR 1.69, 95% CI 1.16–2.48; $P = 0.007$). In eICU, after further adjustment for peri-ICU interventions, FiO_2 0.61–0.80 and > 0.80 were both associated with higher PPC risk (OR 1.51, 95% CI 1.13–2.03; $P = 0.005$ and OR 2.39, 95% CI 1.66–3.44; $P < 0.001$, respectively). Continuous exposure analysis showed that each 0.1 increase in FiO_2 was associated with increased PPC risk in MIMIC-IV (fully adjusted OR 1.13, 95% CI 1.05–1.21; $P = 0.001$) and eICU (Model 4 OR 1.25, 95% CI 1.16–1.35; $P < 0.001$). RCS analyses demonstrated significant overall associations in both cohorts without significant nonlinearity.

Conclusions

Among postoperative ICU patients undergoing CABG, higher early postoperative FiO_2 exposure was associated with an increased risk of PPCs. This association was consistent across multivariable adjustment, continuous exposure analysis, RCS analysis, propensity score weighting, and external validation. These findings support individualized oxygen titration and avoidance of unnecessary high FiO_2 exposure after CABG when adequate oxygenation can be maintained.

Introduction

Coronary artery bypass grafting (CABG) remains a major surgical treatment for complex coronary artery disease. Although advances in perioperative anesthesia, cardiopulmonary bypass techniques, and postoperative intensive care have improved outcomes, postoperative pulmonary complications (PPCs) remain clinically important after CABG[1,2]. PPCs may lead to prolonged mechanical ventilation, reintubation, pneumonia, longer ICU and hospital stays, and increased healthcare burden[3]. Patients undergoing CABG often have multiple comorbidities, including heart failure, diabetes, chronic kidney disease, and chronic obstructive pulmonary disease, and are also exposed to perioperative inflammatory responses, fluid shifts, atelectasis, and mechanical ventilation, all of which may increase pulmonary vulnerability[4].

Oxygen therapy is a fundamental component of postoperative ICU management after CABG. In mechanically ventilated patients, increasing the fraction of inspired oxygen (FiO_2) improves arterial oxygenation and reduces the risk of hypoxemia[5]. However, higher FiO_2 exposure may not be benign. Hyperoxia may promote oxidative stress, absorption atelectasis, alveolar epithelial and endothelial injury, inflammatory activation, and pulmonary microvascular dysfunction, potentially impairing postoperative pulmonary recovery[6]. During the early postoperative period after CABG, patients frequently experience dynamic changes in oxygenation, ventilation, and hemodynamics; therefore, early FiO_2 exposure may be closely related to subsequent pulmonary outcomes[7].

Evidence regarding the association between early postoperative FiO_2 exposure and PPCs after CABG remains limited. Previous studies have often focused on perioperative oxygen exposure in relation to surgical site infection, myocardial injury, or mortality, whereas real-world evidence specifically addressing early ICU FiO_2 exposure and a composite PPC outcome after CABG is sparse[8]. In addition, FiO_2 can be examined both as a clinically categorized exposure and as a continuous variable reflecting dose-response effects, but its potential dose-response relationship and external reproducibility have not been fully evaluated[9]. Because postoperative FiO_2 is influenced by illness severity, oxygenation status, ventilatory parameters, and clinical decision-making, this association is also prone to indication bias and baseline imbalance.

The MIMIC-IV database provides detailed ICU monitoring, treatment, laboratory, and outcome data and is well suited for evaluating early postoperative FiO_2 exposure after CABG[10]. The eICU database, derived from multiple centers, enables external validation of findings across different ICU settings[11]. Therefore, this study aimed to evaluate the association between early postoperative FiO_2 exposure and PPC risk after CABG using MIMIC-IV as the derivation cohort and eICU as the external validation cohort. We hypothesized that higher early postoperative FiO_2 exposure would be associated with increased PPC risk after adjustment for demographics, comorbidities, ventilatory parameters, illness severity, and peri-ICU interventions.

Methods

Study design and data sources

This retrospective cohort study used two publicly available critical care databases. MIMIC-IV 3.1 was used as the derivation cohort, and the eICU Collaborative Research Database was used for external validation. Both databases contain de-identified ICU data, including demographics, diagnoses, vital signs, laboratory tests, treatments, and outcomes. Because the databases are de-identified and publicly available, this secondary analysis did not involve identifiable patient information.

Study population

In MIMIC-IV, we first identified patients who underwent CABG and were admitted to the ICU after surgery. A total of 6,568 postoperative CABG ICU patients were initially screened. Patients were excluded if they had an ICU length of stay < 24 h, underwent concomitant non-CABG surgery, had missing FiO_2 records within the first 6 h after ICU admission, were younger than 18 years, had no record of endotracheal intubation, or had repeated ICU admissions, in which case only the first eligible postoperative ICU stay was retained. The final MIMIC-IV cohort included 5,457 patients. The eICU validation cohort was constructed using a comparable strategy, and 4,521 patients were included.

Exposure definition

The primary exposure was early postoperative FiO_2. For each patient, FiO_2 records during the first 6 h after ICU admission were used to calculate mean FiO_2. The main exposure was categorized into three clinically relevant groups: FiO_2 ≤0.60, FiO_2 0.61–0.80, and FiO_2 >0.80, with FiO_2 ≤0.60 used as the reference group. In MIMIC-IV, the three groups included 817, 3,223, and 1,417 patients, respectively; in eICU, the corresponding numbers were 3,400, 793, and 328.

In additional analyses, FiO_2 was modeled as a continuous variable per 0.1 increase. Restricted cubic spline analysis was performed to evaluate the dose-response relationship between continuous FiO_2 exposure and PPC risk, using FiO_2=0.60 as the reference level.

Outcome definition

The primary outcome was a composite of postoperative pulmonary complications. PPC was defined as the occurrence of any of the following events during the postoperative ICU stay: prolonged mechanical ventilation > 48 h, reintubation, or pneumonia. Patients with at least one of these events were classified as having PPC. The same composite outcome definition was applied as consistently as possible in the MIMIC-IV and eICU cohorts.

Covariates

Covariates were selected based on clinical relevance, prior knowledge, and data availability. Demographic variables included age, sex, weight, height, body mass index (BMI), and race. Baseline comorbidities included

chronic obstructive pulmonary disease (COPD), congestive heart failure (CHF), chronic kidney disease (CKD), diabetes, and hypertension.

Early physiological and ventilatory variables included positive end-expiratory pressure (PEEP), heart rate, and mean arterial pressure during the first 6 h after ICU admission. Laboratory variables included early postoperative lactate, hemoglobin, creatinine, and white blood cell count. In MIMIC-IV, skewed variables such as lactate, creatinine, and white blood cell count were log-transformed in regression models. In eICU, acute physiology score and the lowest P/F ratio within 24 h were additionally extracted. Peri-ICU intervention variables included vasoactive drug use, transfusion, and renal replacement therapy (RRT), and were available for further adjustment in the eICU validation cohort.

Statistical analysis

Continuous variables are presented as mean ± standard deviation or median (interquartile range), depending on distribution. Categorical variables are presented as counts and percentages. Between-group comparisons across FiO_2 categories were performed using one-way analysis of variance or the Kruskal-Wallis test for continuous variables and the chi-square or Fisher exact test for categorical variables, as appropriate. PPC incidence was reported as counts, percentages, and 95% confidence intervals. The chi-square test was used to compare PPC incidence across FiO_2 groups, and the Cochran-Armitage trend test was used to assess ordered trends.

Multivariable logistic regression was used to evaluate the association between FiO_2 exposure and PPCs. Results are presented as odds ratios (ORs) and 95% confidence intervals (CIs). Model 1 was unadjusted. Model 2 adjusted for demographic variables and baseline comorbidities, including age, sex, BMI, race, COPD, CHF, CKD, diabetes, and hypertension. Model 3 further adjusted for early postoperative physiological status, ventilatory parameters, and laboratory variables. In MIMIC-IV, Model 3 included PEEP, heart rate, mean arterial pressure, lactate, hemoglobin, creatinine, and white blood cell count. In eICU, Model 3 included acute physiology score, PEEP, heart rate, mean arterial pressure, and P/F ratio according to data availability. Model 4 further adjusted for peri-ICU interventions, including vasoactive drugs, transfusion, and RRT. Because these intervention variables were not completely available in the current MIMIC-IV analysis dataset, Model 4 was estimated primarily in the eICU validation cohort.

Continuous FiO_2 exposure was assessed per 0.1 increase using the same stepwise adjustment strategy. Restricted cubic spline models were used to assess the overall and nonlinear associations between continuous FiO_2 and PPC risk after covariate adjustment. To further reduce baseline imbalance and indication bias, propensity score analyses were performed in MIMIC-IV. Generalized propensity scores for the three-level FiO_2 exposure were estimated using multinomial logistic regression with baseline covariates only, and generalized overlap weighting was applied. Covariate balance was assessed using absolute standardized mean differences (SMDs), with SMD < 0.10 considered acceptable. As a sensitivity analysis, the extreme FiO_2 groups (> 0.80 vs ≤ 0.60) were compared using stabilized inverse probability of treatment weighting (IPTW). Prespecified subgroup analyses were performed in the binary IPTW sensitivity cohort according to age (< 65 vs ≥ 65 years), COPD status, and obesity status (BMI < 30 vs ≥ 30 kg/m²). Boruta feature selection was used as an exploratory analysis to evaluate the relative predictive importance of

candidate variables for PPCs. All statistical tests were two-sided, and $P < 0.05$ was considered statistically significant. Analyses were performed using Python.

Results

Study population

In MIMIC-IV version 3.1, 6,568 postoperative CABG ICU patients were initially screened (Fig. 1a). After applying the prespecified exclusion criteria, 5,457 patients were included in the derivation cohort. According to early postoperative mean FiO_2, 817 patients were assigned to the FiO_2 ≤0.60 group, 3,223 to the 0.61–0.80 group, and 1,417 to the > 0.80 group. The eICU external validation cohort included 4,521 patients (Fig. 1b), of whom 3,400, 793, and 328 were assigned to the FiO_2 ≤0.60, 0.61–0.80, and > 0.80 groups, respectively.

Baseline characteristics in the MIMIC-IV cohort

Baseline characteristics according to early postoperative FiO_2 group are shown in Table 1. Several baseline and early ICU variables differed across FiO_2 groups. Compared with lower FiO_2 groups, patients in the higher FiO_2 group tended to have higher BMI, PEEP, heart rate, lactate, creatinine, and white blood cell count. The prevalence of CHF, CKD, and diabetes also differed across groups. These differences indicated baseline imbalance among exposure groups and supported the use of multivariable adjustment and propensity score methods.

Table 1
Baseline characteristics according to early postoperative FiO_2 group in the MIMIC-IV cohort.

Characteristic	Total	FiO_2 ≤0.60	FiO_2 0.61–0.80	FiO_2 >0.80	P value
No	5457	817	3223	1417	
Age, years	69.00 (61.00, 75.00)	68.00 (61.00, 76.00)	69.00 (62.00, 75.00)	69.00 (61.00, 76.00)	0.817
Weight, kg	84.00 (73.50, 97.00)	80.00 (70.00, 91.00)	84.00 (73.90, 96.90)	87.00 (76.00, 100.20)	< 0.001
Height, cm	173.00 (165.00, 178.00)	173.00 (165.00, 178.00)	173.00 (165.00, 178.00)	173.00 (165.00, 178.00)	0.388
BMI, kg/m²	28.40 (25.26, 32.18)	27.05 (24.22, 30.31)	28.38 (25.34, 31.96)	29.34 (25.88, 33.31)	< 0.001
PEEP, first 6 h, cmH2O	5.00 (5.00, 5.00)	5.00 (5.00, 5.00)	5.00 (5.00, 5.00)	5.00 (5.00, 6.25)	< 0.001
Heart rate, first 6 h, bpm	79.70 (74.50, 84.15)	79.50 (74.24, 84.00)	79.39 (74.29, 83.53)	80.00 (75.20, 85.56)	< 0.001
MAP, first 6 h, mmHg	75.36 (70.67, 80.08)	76.15 (71.40, 80.55)	75.40 (70.85, 80.00)	74.91 (69.67, 80.00)	0.001
Lactate, first 24 h	2.50 (2.00, 3.20)	2.40 (1.90, 3.10)	2.40 (1.90, 3.10)	2.70 (2.10, 3.50)	< 0.001
Hemoglobin, first 24 h	8.70 (7.50, 9.90)	8.80 (7.60, 9.80)	8.80 (7.60, 9.90)	8.60 (7.30, 10.00)	0.295
Creatinine, first 24 h	0.90 (0.80, 1.20)	0.90 (0.80, 1.10)	0.90 (0.80, 1.10)	1.00 (0.80, 1.20)	< 0.001
WBC, first 24 h	15.70 (12.60, 19.70)	15.00 (12.00, 18.80)	15.70 (12.40, 19.50)	16.40 (13.10, 20.80)	< 0.001
Sex, n (%)	Sex, n (%)	Sex, n (%)	Sex, n (%)	Sex, n (%)	Sex, n (%)
Male	4273 (78.30%)	624 (76.38%)	2533 (78.59%)	1116 (78.76%)	0.347
Female	1184 (21.70%)	193 (23.62%)	690 (21.41%)	301 (21.24%)	
Race, n (%)	Race, n (%)	Race, n (%)	Race, n (%)	Race, n (%)	Race, n (%)
White	3859 (70.72%)	560 (68.54%)	2298 (71.30%)	1001 (70.64%)	0.127
Black	214 (3.92%)	32 (3.92%)	129 (4.00%)	53 (3.74%)	

Note: Continuous variables are presented as median (Q1, Q3) unless otherwise indicated; categorical variables are presented as n (%). P values were calculated using the Kruskal-Wallis test or one-way ANOVA for continuous variables and the chi-square test for categorical variables, as appropriate. Abbreviations: FiO_2, fraction of inspired oxygen; PEEP, positive end-expiratory pressure; MAP, mean arterial pressure; WBC, white blood cell count; COPD, chronic obstructive pulmonary disease; CHF, congestive heart failure; CKD, chronic kidney disease.

Characteristic	Total	FiO_2 ≤0.60	FiO_2 0.61–0.80	FiO_2 >0.80	P value
Asian	125 (2.29%)	27 (3.30%)	77 (2.39%)	21 (1.48%)	
Hispanic	170 (3.12%)	29 (3.55%)	102 (3.16%)	39 (2.75%)	
Other/Unknown	1089 (19.96%)	169 (20.69%)	617 (19.14%)	303 (21.38%)	
Comorbidities, n (%)	Comorbidities, n (%)	Comorbidities, n (%)	Comorbidities, n (%)	Comorbidities, n (%)	Comorbidities, n (%)
COPD	364 (6.67%)	48 (5.88%)	217 (6.73%)	99 (6.99%)	0.583
CHF	1239 (22.70%)	149 (18.24%)	672 (20.85%)	418 (29.50%)	< 0.001
CKD	1029 (18.86%)	133 (16.28%)	595 (18.46%)	301 (21.24%)	0.010
Diabetes	2094 (38.37%)	278 (34.03%)	1220 (37.85%)	596 (42.06%)	< 0.001
Hypertension	4599 (84.28%)	672 (82.25%)	2710 (84.08%)	1217 (85.89%)	0.068

Note: Continuous variables are presented as median (Q1, Q3) unless otherwise indicated; categorical variables are presented as n (%). P values were calculated using the Kruskal-Wallis test or one-way ANOVA for continuous variables and the chi-square test for categorical variables, as appropriate. Abbreviations: FiO_2, fraction of inspired oxygen; PEEP, positive end-expiratory pressure; MAP, mean arterial pressure; WBC, white blood cell count; COPD, chronic obstructive pulmonary disease; CHF, congestive heart failure; CKD, chronic kidney disease.

FiO_2 categories and PPC incidence in MIMIC-IV

In the MIMIC-IV cohort, the incidence of PPCs increased across early postoperative FiO_2 categories. PPC occurred in 5.51% (45/817) of patients in the FiO_2 ≤0.60 group, 8.10% (261/3,223) in the 0.61–0.80 group, and 14.61% (207/1,417) in the > 0.80 group. The between-group difference and the ordered trend were statistically significant ($P < 0.001$; Fig. 2).

Multivariable logistic regression in MIMIC-IV

In the unadjusted model, compared with FiO_2 ≤0.60, both FiO_2 0.61–0.80 and FiO_2 >0.80 were associated with higher odds of PPCs (OR 1.44, 95% CI 1.02–2.04; P = 0.038 and OR 2.71, 95% CI 1.89–3.87; $P < 0.001$, respectively). After adjustment for demographics, BMI, race, and baseline comorbidities, the associations remained significant (OR 1.43, 95% CI 1.00–2.03; P = 0.047 and OR 2.41, 95% CI 1.67–3.48; $P < 0.001$).

In the fully adjusted MIMIC-IV model, FiO_2 >0.80 remained significantly associated with increased PPC risk (OR 1.69, 95% CI 1.16–2.48; P = 0.007), whereas FiO_2 0.61–0.80 was no longer statistically significant (OR 1.30, 95% CI 0.91–1.86; $P = 0.150$). These findings suggest that higher early postoperative FiO_2 exposure, particularly FiO_2 >0.80, was independently associated with PPC risk in MIMIC-IV (Fig. 3).

Continuous FiO_2 exposure and dose-response relationship

When FiO_2 was modeled as a continuous exposure, each 0.1 increase in FiO_2 was associated with increased PPC risk in MIMIC-IV. The ORs per 0.1 increase were 1.27 (95% CI 1.19–1.35; $P < 0.001$) in the unadjusted

model, 1.23 (95% CI 1.15–1.32; *P* < 0.001) after adjustment for demographics and comorbidities, and 1.13 (95% CI 1.05–1.21; P = 0.001) in the fully adjusted model (Fig. 4).

Consistent findings were observed in the eICU external validation cohort. Each 0.1 increase in FiO_2 was associated with higher odds of PPCs across all models, with an OR of 1.25 (95% CI 1.16–1.35; *P* < 0.001) in the fully adjusted Model 4 (Fig. 5). RCS analyses showed significant overall associations between FiO_2 and PPC risk in both cohorts (both P-overall ≤ 0.001), without significant nonlinear associations (MIMIC-IV: P-non-linear = 0.122; eICU: P-non-linear = 0.362). Using FiO_2=0.60 as the reference, PPC risk generally increased at higher FiO_2 levels in both cohorts (Fig. 6).

External validation in eICU

In the eICU validation cohort, PPC incidence also increased across FiO_2 groups. The incidence was 9.41% (320/3,400) in the FiO_2 ≤0.60 group, 14.25% (113/793) in the 0.61–0.80 group, and 26.52% (87/328) in the > 0.80 group, with significant between-group differences and an ordered trend (both *P* < 0.001; Fig. 7).

Multivariable logistic regression in eICU confirmed the direction of the MIMIC-IV findings. In the unadjusted model, FiO_2 0.61–0.80 and > 0.80 were associated with increased PPC risk (OR 2.04, 95% CI 1.56–2.67; *P* < 0.001 and OR 4.64, 95% CI 3.39–6.36; *P* < 0.001, respectively). After further adjustment for demographics, comorbidities, illness severity, ventilatory parameters, oxygenation status, and peri-ICU interventions, both associations remained significant (OR 1.51, 95% CI 1.13–2.03; P = 0.005 and OR 2.39, 95% CI 1.66–3.44; *P* < 0.001, respectively). Comparative results from MIMIC-IV and eICU are shown in Fig. 8.

Sensitivity and exploratory analyses

Propensity score-based sensitivity analyses in MIMIC-IV further supported the robustness of the main findings. After overlap weighting, covariate balance improved substantially, and the weighted incidence of PPCs increased monotonically across FiO_2 groups: 5.52% in the ≤ 0.60 group, 8.27% in the 0.61–0.80 group, and 12.66% in the > 0.80 group. Compared with FiO_2 ≤0.60, both FiO_2 0.61–0.80 (OR 1.54, 95% CI 1.19–2.00; *P* = 0.001) and FiO_2 >0.80 (OR 2.48, 95% CI 1.94–3.16; *P* < 0.001) remained associated with higher PPC risk. Binary IPTW sensitivity analysis comparing FiO_2 >0.80 with ≤ 0.60 showed a consistent direction of effect. Additional subgroup and exploratory Boruta feature importance analyses are provided in the Supplementary Material.

Discussion

Principal findings

This study systematically evaluated the association between early postoperative FiO_2 exposure and PPC risk among ICU patients after CABG using MIMIC-IV and externally validated the findings in eICU. The main findings were as follows. First, PPC incidence increased stepwise across higher FiO_2 categories in MIMIC-IV. Second, higher FiO_2 exposure, particularly FiO_2 >0.80, remained associated with increased PPC risk after multivariable adjustment. Third, continuous exposure analysis showed that each 0.1 increase in FiO_2 was

associated with higher PPC risk. Fourth, RCS analyses demonstrated significant overall dose-response associations without significant nonlinearity. Fifth, the eICU cohort reproduced the direction of the findings, and the association persisted after further adjustment for peri-ICU interventions. Finally, propensity score weighting and sensitivity analyses supported the robustness of the results.

Clinical interpretation

Postoperative oxygen therapy is routinely used after CABG to maintain adequate oxygenation and prevent hypoxemia[12]. However, the present findings suggest that higher early FiO_2 exposure is not necessarily associated with better pulmonary outcomes. In MIMIC-IV, the incidence of PPCs in the FiO_2 >0.80 group was approximately 2.7-fold higher than that in the FiO_2 ≤0.60 group. Although part of this association may reflect underlying illness severity and greater ventilatory support requirements, the association persisted after adjustment for measured demographics, comorbidities, ventilatory parameters, physiological status, and laboratory variables. The eICU validation results further strengthen the external consistency of this association.

The intermediate FiO_2 group showed attenuation after full adjustment in MIMIC-IV, whereas it remained significant in eICU. This difference may be related to differences in case mix, baseline PPC risk, variable availability, and clinical practice patterns between the two databases. Nevertheless, both cohorts consistently demonstrated the highest risk among patients exposed to FiO_2 >0.80.

Potential mechanisms

The observed association is biologically plausible. Excessive oxygen exposure may promote oxidative stress and reactive oxygen species generation, leading to alveolar epithelial and endothelial injury, increased alveolar-capillary permeability, and delayed pulmonary recovery[6]. High FiO_2 may also increase the risk of absorption atelectasis by reducing alveolar nitrogen content, particularly after anesthesia, surgery, and mechanical ventilation[9]. In patients after CABG, sternotomy, postoperative pain, impaired diaphragmatic function, changes in lung compliance, and inflammatory responses may further increase susceptibility to atelectasis, ventilation-perfusion mismatch, pneumonia, reintubation, and prolonged mechanical ventilation[13].

At the same time, high FiO_2 may also serve as a marker of more severe postoperative illness, poorer oxygenation, or greater respiratory support[5,9]. Therefore, the results should be interpreted as associations rather than proof of causality. The persistence of the association after multivariable adjustment and propensity score weighting suggests that measured confounding alone is unlikely to fully explain the findings, but residual confounding remains possible.

External validation and robustness

The external validation in eICU is an important strength of this study. MIMIC-IV and eICU differ in data sources, patient populations, clinical practice patterns, and variable structures. Despite these differences, eICU reproduced the graded increase in PPC incidence and the positive association between higher FiO_2 exposure and PPC risk. Propensity score analyses in MIMIC-IV also improved covariate balance and yielded

consistent findings. These results suggest that the association between high early postoperative FiO_2 exposure and PPC risk is not dependent on a single database or a single modeling strategy.

Clinical implications

These findings have implications for postoperative oxygen management after CABG. Oxygen therapy should aim to avoid hypoxemia while minimizing unnecessary hyperoxia[14]. High FiO_2 remains appropriate for patients with severe hypoxemia, hemodynamic instability, or inadequate oxygen reserve. However, once adequate oxygenation is achieved, prolonged maintenance of high FiO_2 may not be beneficial and may be associated with higher pulmonary risk[13]. Dynamic FiO_2 titration, together with appropriate PEEP, lung recruitment strategies, analgesia, early extubation, and pulmonary rehabilitation, may help optimize postoperative respiratory care after CABG[15,16].

Limitations

This study has limitations. First, as a retrospective observational study, it cannot establish causality, and unmeasured or residual confounding may remain despite multivariable adjustment and propensity score analyses. Second, FiO_2 exposure was based on early postoperative ICU records and may not fully capture intraoperative oxygen exposure, dynamic postoperative FiO_2 changes, oxygen exposure duration, or weaning strategies. Third, the composite PPC outcome was based on database records and may be affected by documentation, coding, and practice differences. Fourth, MIMIC-IV and eICU differ in variable availability and definitions; in particular, peri-ICU intervention variables were unavailable in the current MIMIC-IV analysis dataset, so Model 4 was estimated primarily in eICU. Finally, potentially important intraoperative factors such as cardiopulmonary bypass duration, aortic cross-clamp time, intraoperative ventilation strategy, blood loss, and extubation protocols were not fully available. Prospective studies are needed to confirm these findings and define optimal FiO_2 targets after CABG.

Conclusion

In postoperative ICU patients undergoing CABG, higher early postoperative FiO_2 exposure was associated with an increased risk of PPCs. This association was consistent in the MIMIC-IV derivation cohort and the eICU external validation cohort, and was supported by continuous exposure analysis, RCS analysis, propensity score weighting, and sensitivity analyses. These findings suggest that postoperative oxygen management after CABG should not focus solely on preventing hypoxemia, but should also consider avoiding unnecessary high FiO_2 exposure when adequate oxygenation can be maintained. Prospective studies are warranted to determine optimal FiO_2 titration strategies and their effects on pulmonary outcomes after CABG.

Abbreviations

BMI
body mass index
CABG

coronary artery bypass grafting
CHF
congestive heart failure
CI
confidence interval
CKD
chronic kidney disease
COPD
chronic obstructive pulmonary disease
FiO_2
fraction of inspired oxygen
ICU
intensive care unit
IPTW
inverse probability of treatment weighting
MAP
mean arterial pressure
OR
odds ratio
PEEP
positive end-expiratory pressure
PPC
postoperative pulmonary complication
RCS
restricted cubic spline
RRT
renal replacement therapy
SMD
standardized mean difference
WBC
white blood cell count.

Declarations

Ethics approval and consent to participate

Not applicable.

Consent for publication

This manuscript has not been published or presented elsewhere in part or in entirety, and is not under consideration by another journal. All the authors have approved the manuscript and agree with submission to your esteemed journal.

Availability of data and materials

These data were derived from the following resources available in the public domain: https://mimic.mit.edu and http://eicu-crd.mit.edu .

Competing Interests

The authors declare no competing interests.

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Authors' contributions

Fei Gao and Zixiao Kong wrote the main manuscript text and analised dataset. Shuwen Li prepared figures. Sheng Wang prepared tables. All authors reviewed the manuscript.

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Figures

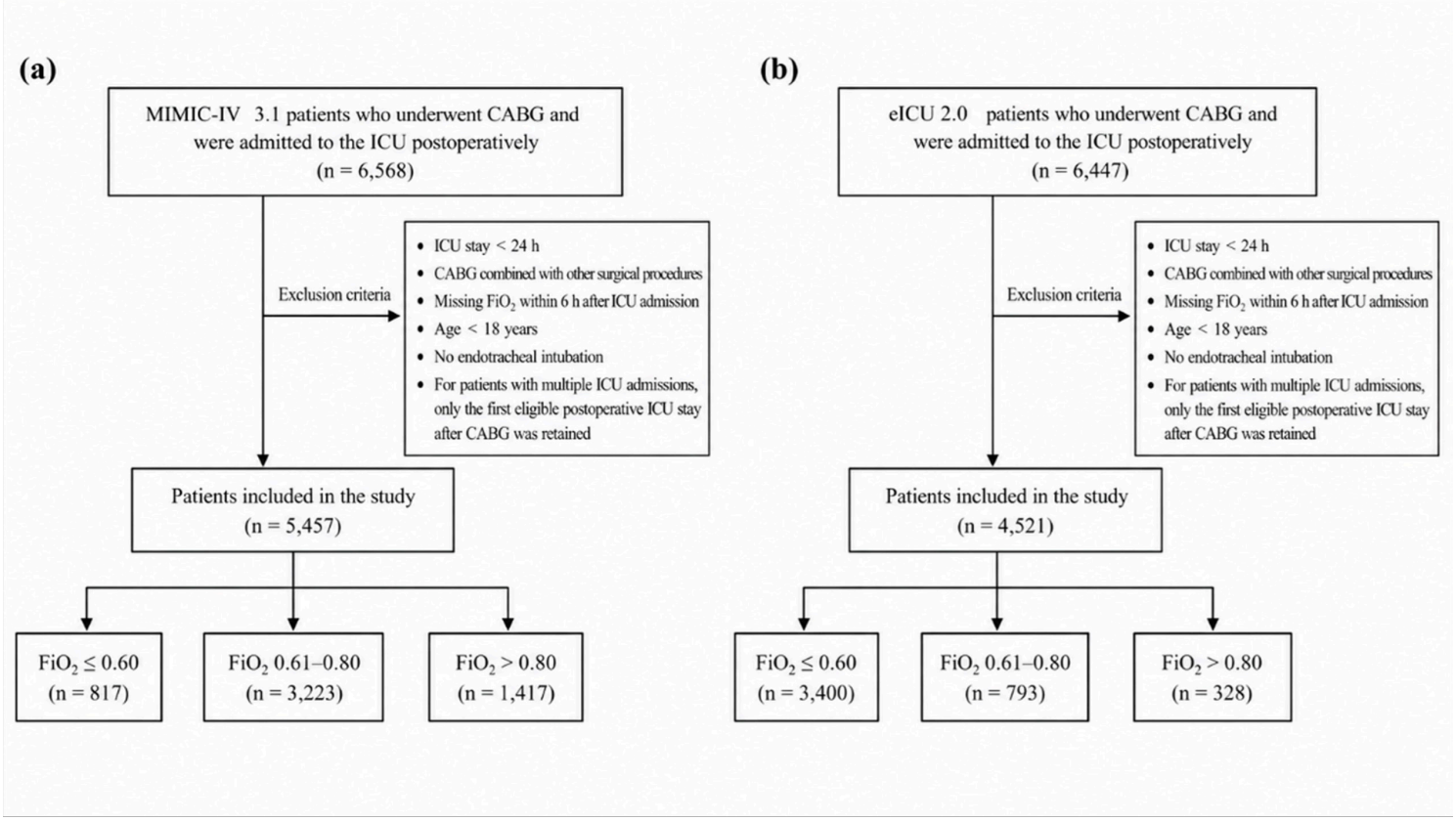


Figure 1

Flowchart of study participants in the MIMIC-IV and eICU databases. (a) MIMIC-IV cohort; (b) eICU external validation cohort. CABG, coronary artery bypass grafting; FiO_2, fraction of inspired oxygen.

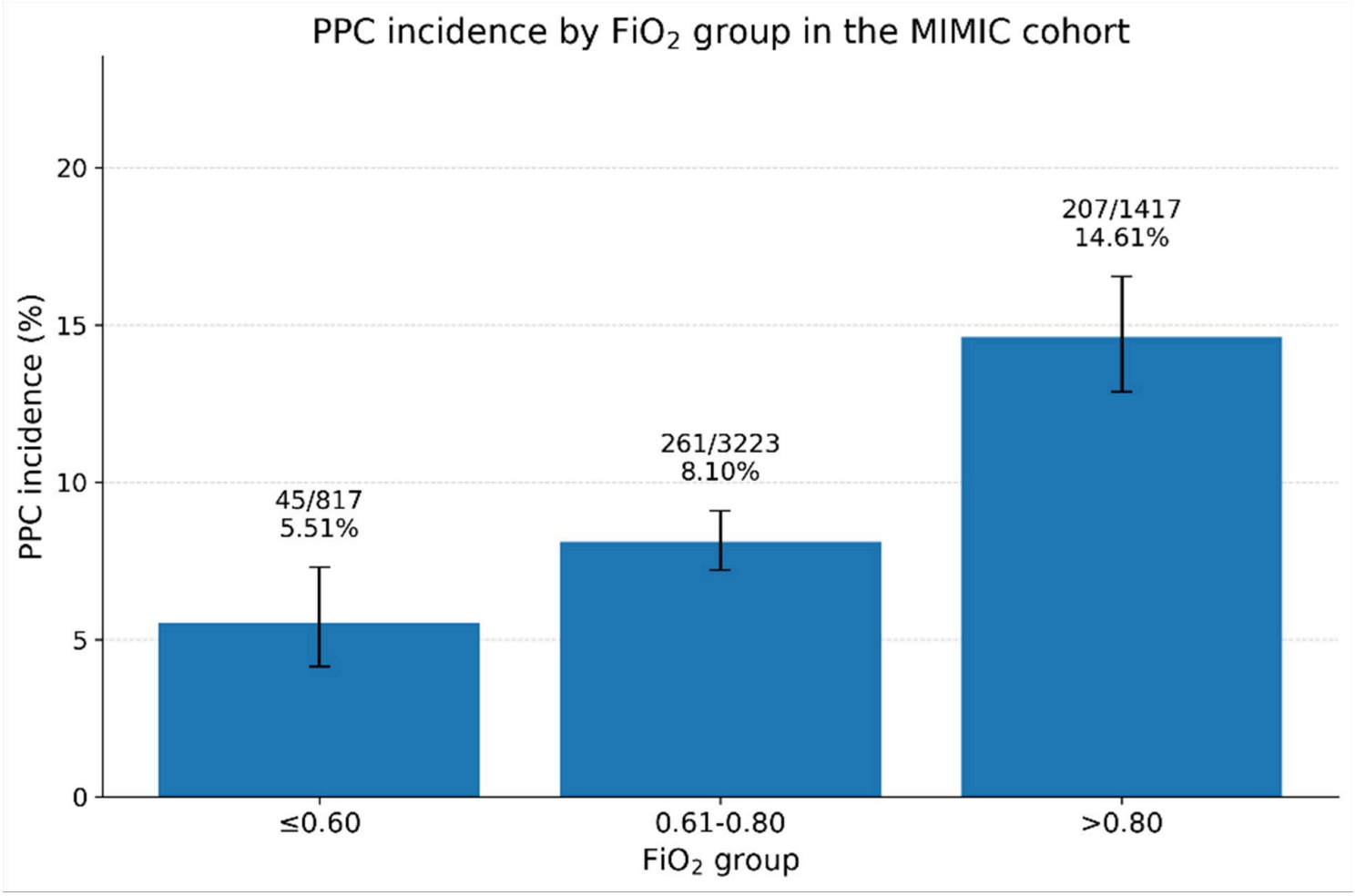


Figure 2

PPC incidence according to early postoperative FiO_2 group in the MIMIC-IV cohort. Bars indicate incidence rates and error bars indicate 95% confidence intervals. FiO_2, fraction of inspired oxygen; PPC, postoperative pulmonary complications.

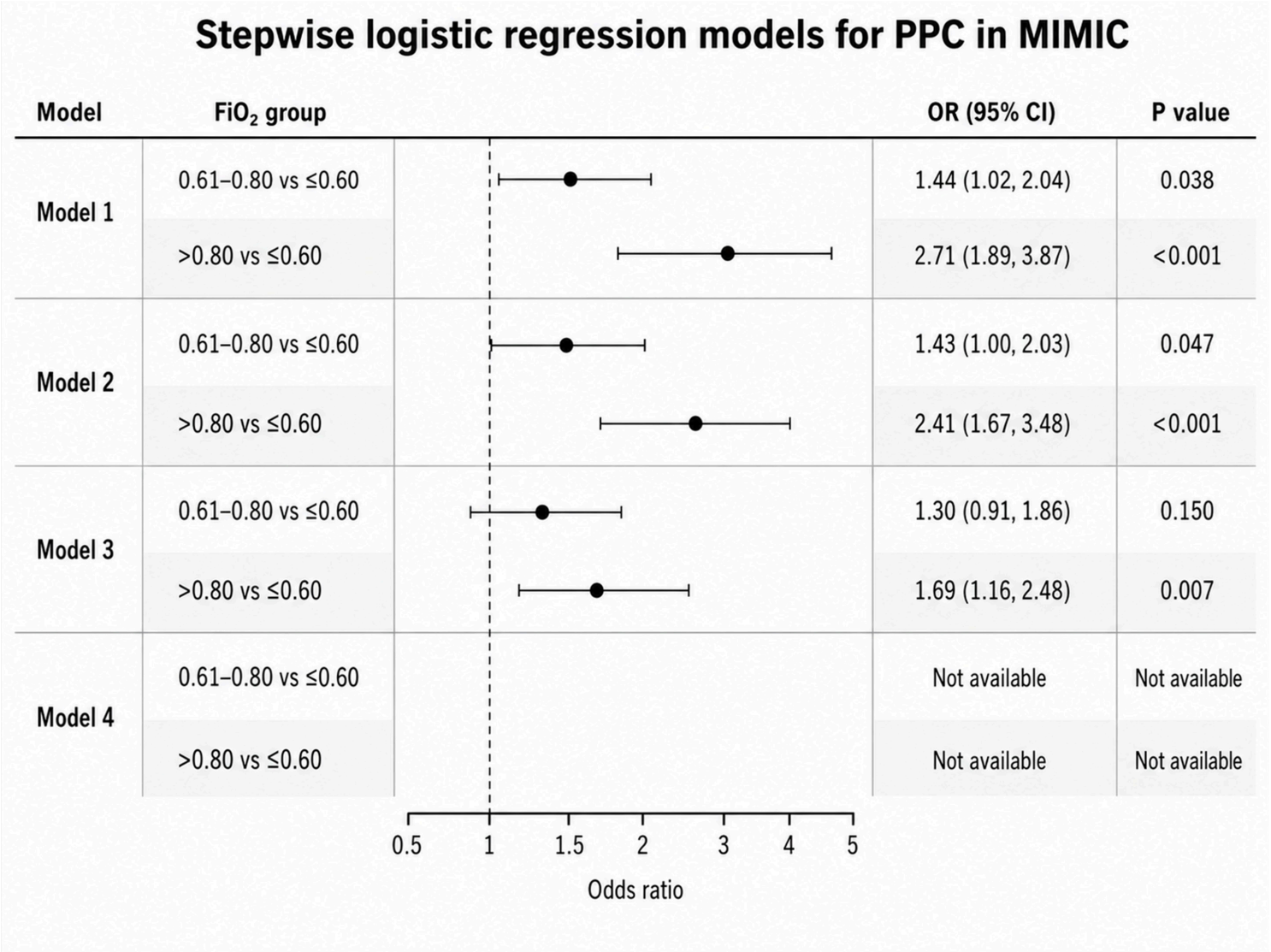


Figure 3

Stepwise logistic regression models for the association between early postoperative FiO_2 group and PPC risk in the MIMIC-IV cohort. FiO_2 ≤0.60 was used as the reference group. Dots indicate ORs and horizontal lines indicate 95% CIs; the vertical dashed line indicates OR=1.

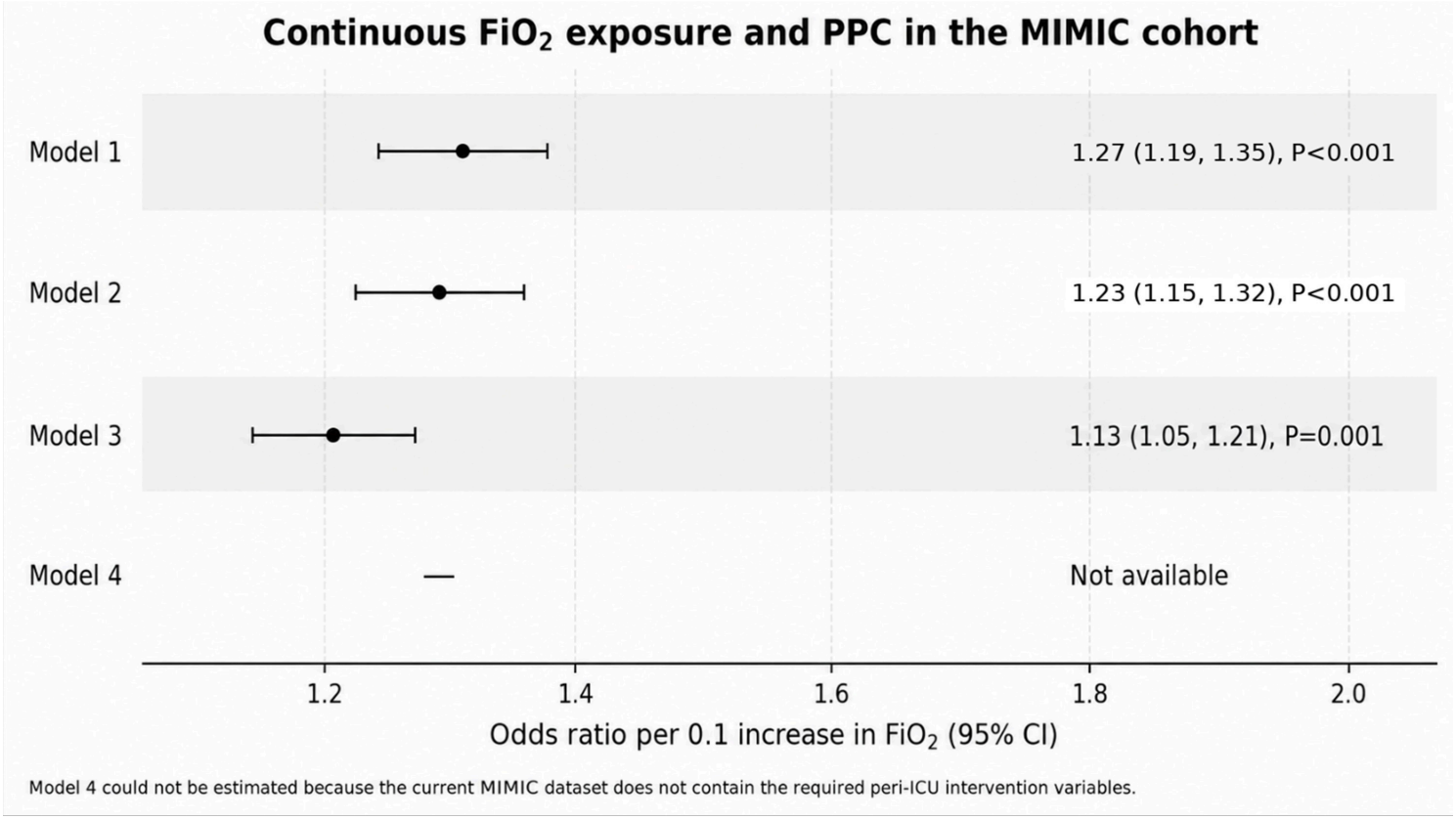


Figure 4

Association between continuous FiO_2 exposure and PPC risk in the MIMIC-IV cohort. ORs are shown per 0.1 increase in FiO_2 across stepwise logistic regression models.

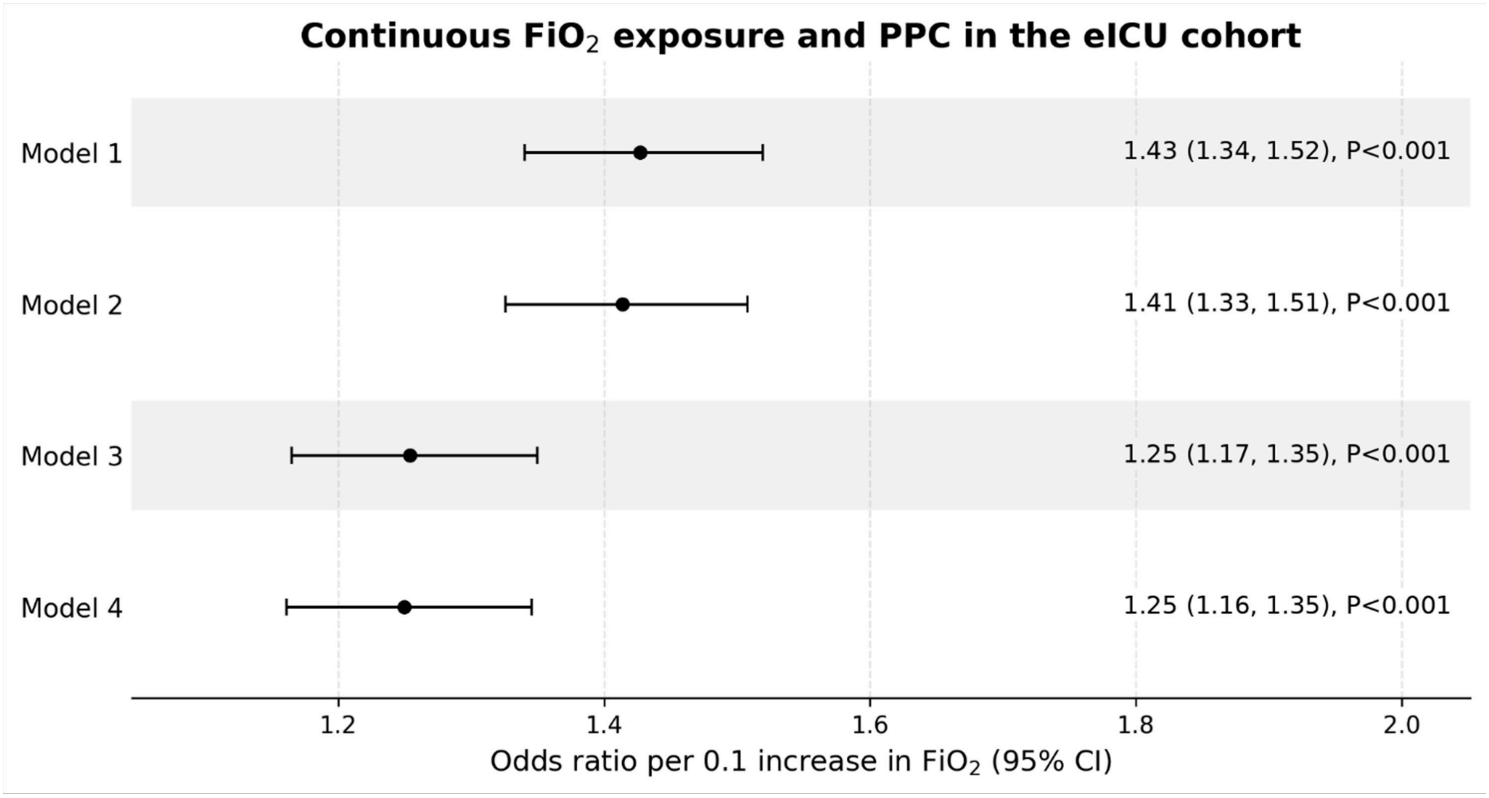


Figure 5

Association between continuous FiO_2 exposure and PPC risk in the eICU cohort. ORs are shown per 0.1 increase in FiO_2 across stepwise logistic regression models.

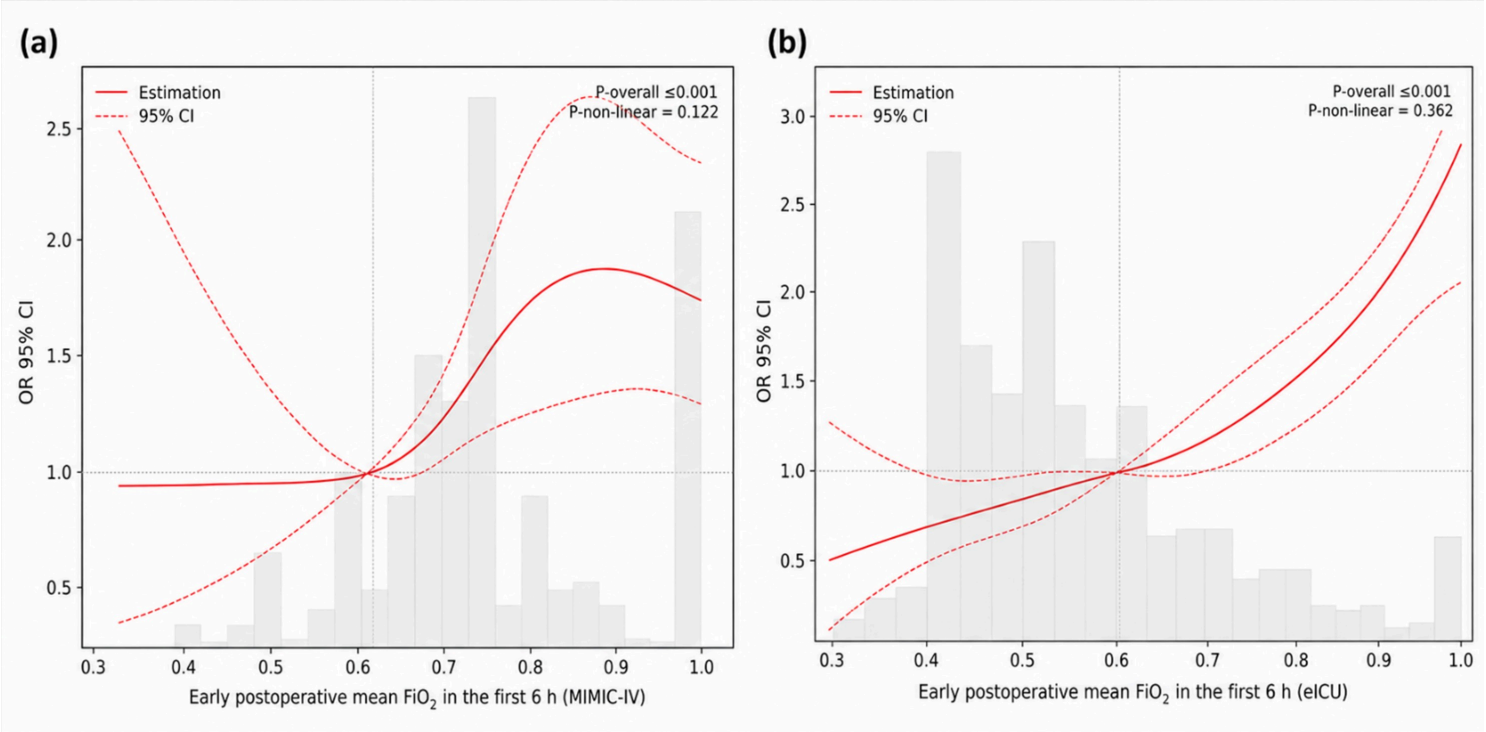


Figure 6

Restricted cubic spline analysis of early postoperative FiO_2 exposure and PPC risk in the MIMIC-IV and eICU cohorts. (a) MIMIC-IV cohort; (b) eICU cohort. Solid red lines represent estimated ORs, dashed red lines represent 95% CIs, and gray bars represent the distribution of FiO_2. FiO_2=0.60 was used as the reference level.

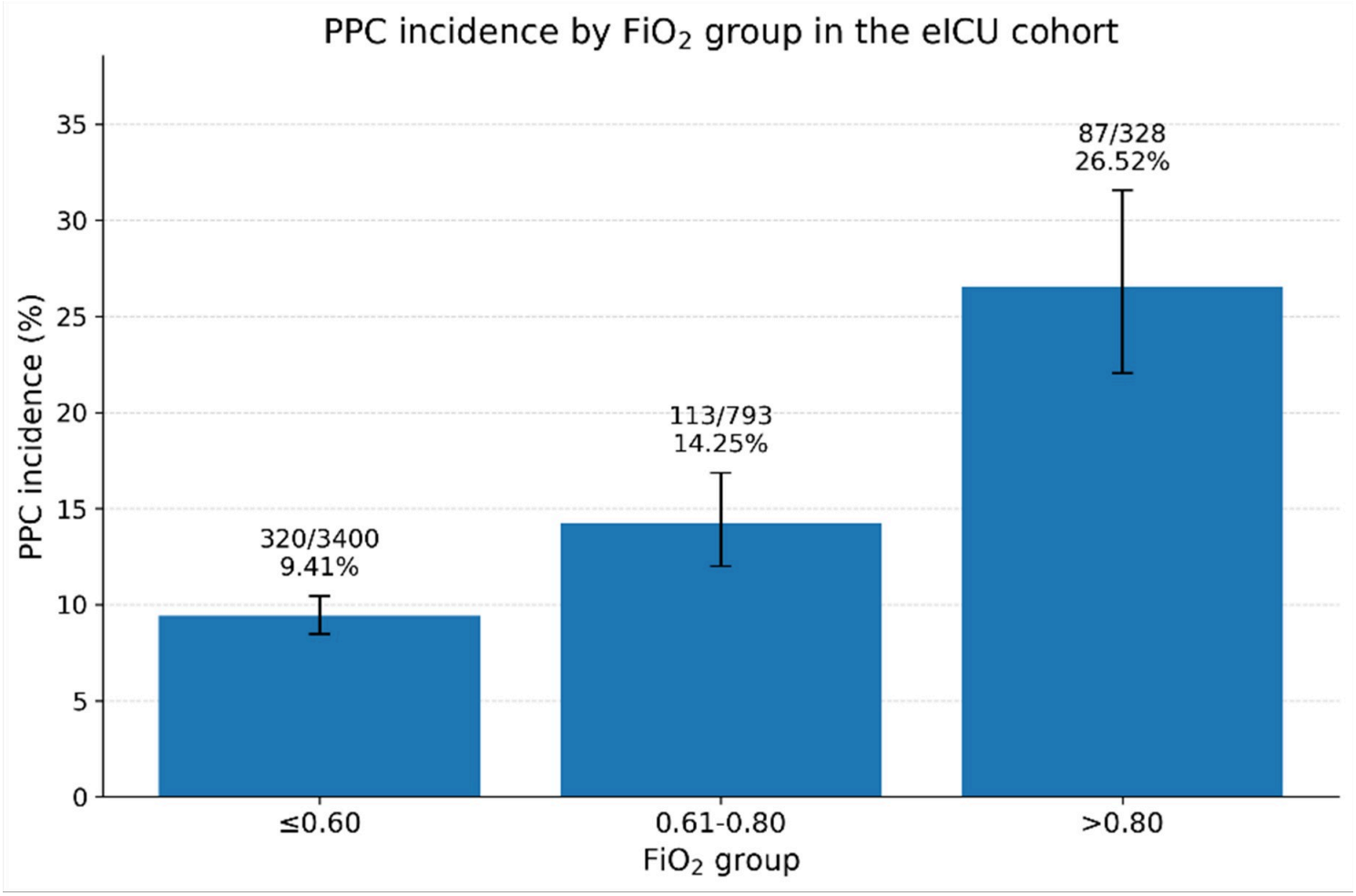


Figure 7

PPC incidence according to early postoperative FiO_2 group in the eICU cohort. Bars indicate incidence rates and error bars indicate 95% confidence intervals.

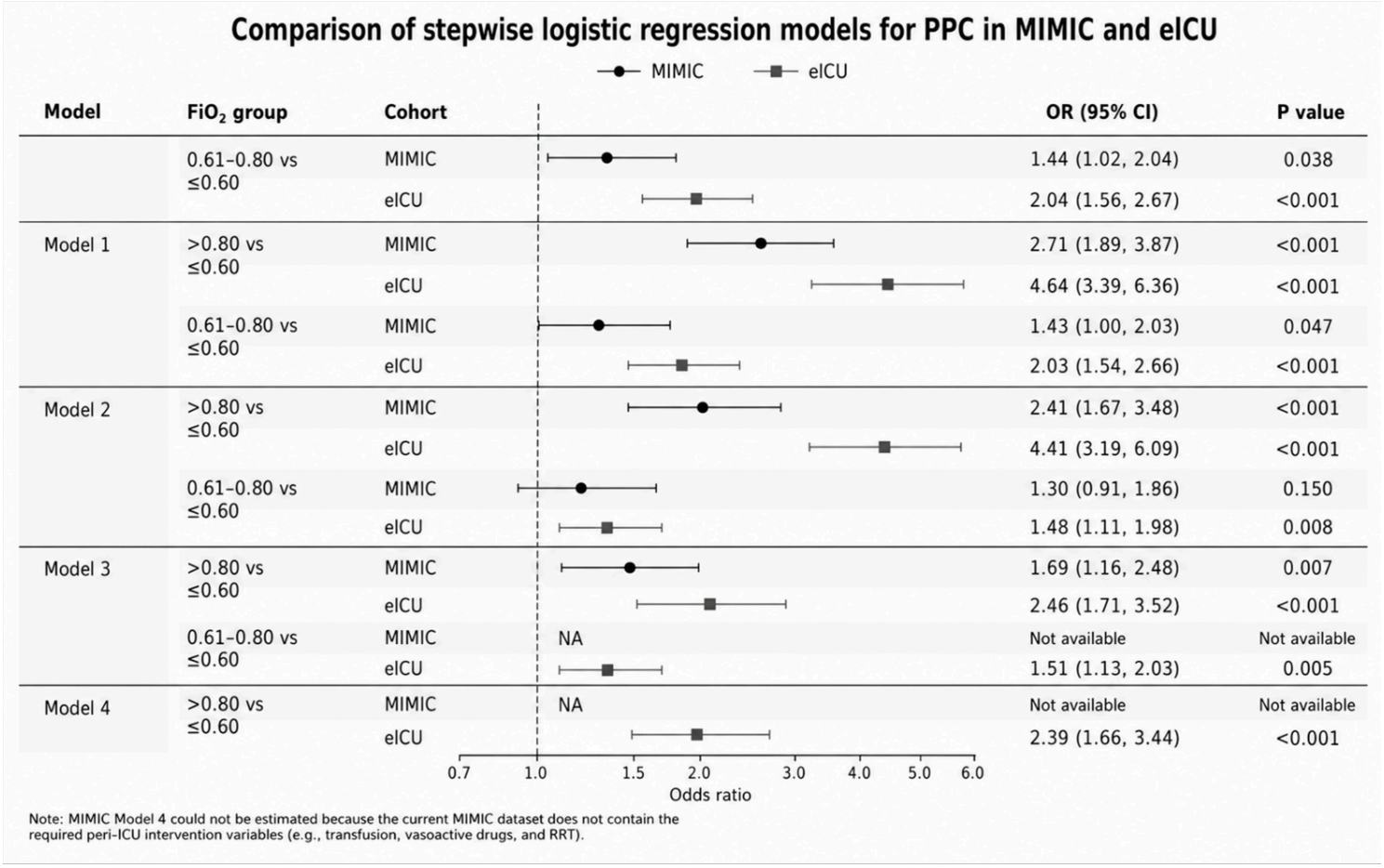


Figure 8

Comparison of stepwise logistic regression models for PPC risk in the MIMIC-IV and eICU cohorts. Circles represent MIMIC-IV estimates and squares represent eICU estimates; horizontal lines indicate 95% CIs. MIMIC-IV Model 4 was not estimated because peri-ICU intervention variables were unavailable in the current MIMIC-IV analysis dataset.

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- Supplement.docx