

Risk Factors and Short-Term Outcomes of Postoperative Pulmonary Complications in Elderly Patients After Cardiopulmonary Bypass

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Objective: The risk factors of postoperative pulmonary complications (PPCs) have been extensively investigated in non-cardiac surgery and non-elderly adult patients undergoing cardiac surgery. However, data on elderly patients after cardiopulmonary bypass (CPB) is limited. This study aimed to evaluate the risk factors and short-term outcomes for PPCs in elderly patients undergoing CPB procedures.

Patients and Methods: Data from 660 patients who underwent CPB over a six-year period at a tertiary care hospital were collected. The primary outcome encompassed the incidence of PPCs, including re-intubation, postoperative mechanical ventilation exceeding 48 hours, pulmonary infection, pleural effusion requiring thoracic drainage, and acute respiratory distress syndrome. Missing data were managed using multiple imputation. Univariate analysis and the multiple logistic regression method were utilized to ascertain independent risk factors for PPCs.

Results: Among the 660 patients, PPCs were observed in 375 individuals (56.82%). Multiple logistic regression identified serum albumin levels <40 g/L, type of surgery, CPB duration >150 minutes, blood transfusion, and intra-aortic balloon pump use before extubation as independent risk factors for PPCs. Patients experiencing PPCs had prolonged mechanical ventilation, extended hospitalization and ICU stays, elevated postoperative mortality, and higher tracheotomy rates compared to those without PPCs.

Conclusion: Elderly patients following CPB displayed a substantially high incidence of PPCs, significantly impacting their prognosis. Additionally, this study identified five prominent risk factors associated with PPCs in this population. These findings enable clinicians to better recognize patients who may benefit from perioperative prevention strategies based on these risk factors.

Keywords: postoperative pulmonary complications, elderly patients, cardiopulmonary bypass, cardiac surgery

Introduction

Postoperative pulmonary complications (PPCs) frequently occur subsequent to cardiac surgery, substantially increasing mortality rates, prolonging stays in the intensive care unit (ICU), extending mechanical ventilation durations, and contributing to elevated healthcare expenditures.¹⁻⁴ Cardiopulmonary bypass (CPB) assumes a critical role in cases of cardiac arrest by diverting the patient's blood from the cardiopulmonary system externally to establish a new circulation.⁵ CPB induces distinctive physiological consequences. Owing to the systemic inflammatory response and ischemia-reperfusion injury, patients become more susceptible to reduced lung function and a heightened incidence of PPCs.

Annually, over 300 million surgical procedures are conducted globally, with this number steadily increasing.^{6,7} As the global population ages, there is a burgeoning trend of elderly patients undergoing open-heart surgery.⁸ Although age is no longer a barrier for surgical candidacy, elderly patients remain susceptible due to various comorbidities.⁹ Besides, despite recognition as a high-risk group,¹⁰⁻¹² limited research has delved into the risk factors and clinical outcomes of PPCs in

elderly patients undergoing CPB. Identification of significant perioperative factors influencing PPCs in this subgroup will assist clinicians in selecting suitable surgical candidates and improving perioperative care.

Material and Methods

Study Design and Population

We conducted a retrospective analysis involving elderly patients who underwent elective cardiac surgery with CPB at Wuhan Union Hospital between January 2014 and December 2019. The elderly population is defined as individuals aged 65 years and above.¹³ Patients who died within 48 hours after surgery or underwent a second thoracotomy were excluded. This study adhered to the principles outlined in the Declaration of Helsinki and received approval from the Ethics Committee of Wuhan Union Hospital (No.2021–0621). Due to the retrospective and anonymized nature of the data, patients' informed consent requirement was waived by the Ethics Committee.

Data Collection

Demographic data and clinical characteristics of patients were obtained through the electronic medical record system. Demographic information encompassed age, gender, body mass index (BMI), drinking history, smoking history, forced expiratory volume in one second/forced vital capacity (FEV1/FVC) ratio, left ventricular ejection fraction (LVEF), and European System for Cardiac Operative Risk Evaluation (EuroScore). Documented comorbidities included hypertension, diabetes, coronary artery disease, myocardial infarction, cerebrovascular disease, pulmonary hypertension, as well as atrial fibrillation. Preoperative medication history covered positive inotropic drug use and antibiotic use. Laboratory tests comprised hemoglobin levels, platelet count, lymphocyte count, neutrophil count, monocyte count, serum albumin, aspartate transaminase, alanine transaminase, serum creatinine, urea nitrogen, along with estimated glomerular filtration rate (eGFR). Intraoperative and postoperative variables included surgical incision, type of surgery, CPB time, aortic cross-clamp time, duration of surgery, duration of anesthesia, blood transfusion, use of intra-aortic balloon pump (IABP) before extubation, together with postoperative complications. Anemia was defined as a hemoglobin level below 130 g/L in the males or below 120 g/L in the females.

Outcome

The primary endpoint of the study was the incidence of PPCs during hospitalization. PPCs specifically refer to re-intubation, postoperative mechanical ventilation lasting more than 48 hours, pulmonary infection, pleural effusion requiring thoracic drainage, and acute respiratory distress syndrome (ARDS). Pulmonary infection was featured by the administration of antibiotic therapy and symptoms such as purulent sputum, alterations in chest radiographs, fever, or an abnormal white blood cell count.¹⁴

Data Analysis

Continuous variables with a normal distribution were presented as mean \pm standard deviation (SD), while those with a skewed distribution were provided as median and interquartile range (IQR). Categorical variables were presented using frequencies and percentages. Continuous variables were analyzed using the *t*-test or Mann–Whitney test, and categorical variables were assessed using the chi-square test or Fisher exact test.

Multiple imputation was employed to address missing data, with a deletion rate of under 15%. Univariate analysis and multivariate logistic regression methods were used on the interpolated data to investigate the independent risk factors for PPCs. To facilitate clinical interpretation, continuous variables were converted into binary variables based on clinical expertise or the Youden's index of the receiver operating characteristic curve. Statistical significance was set at a two-tailed P-value of <0.05 . All data analyses were performed using R software version 4.1.1.

Results

Clinical Characteristics

Among the 668 evaluated patients, three died within 48 hours post-surgery, and five were excluded due to secondary thoracotomy. Consequently, our study included data from 660 patients for analysis. Data deletion primarily involved test

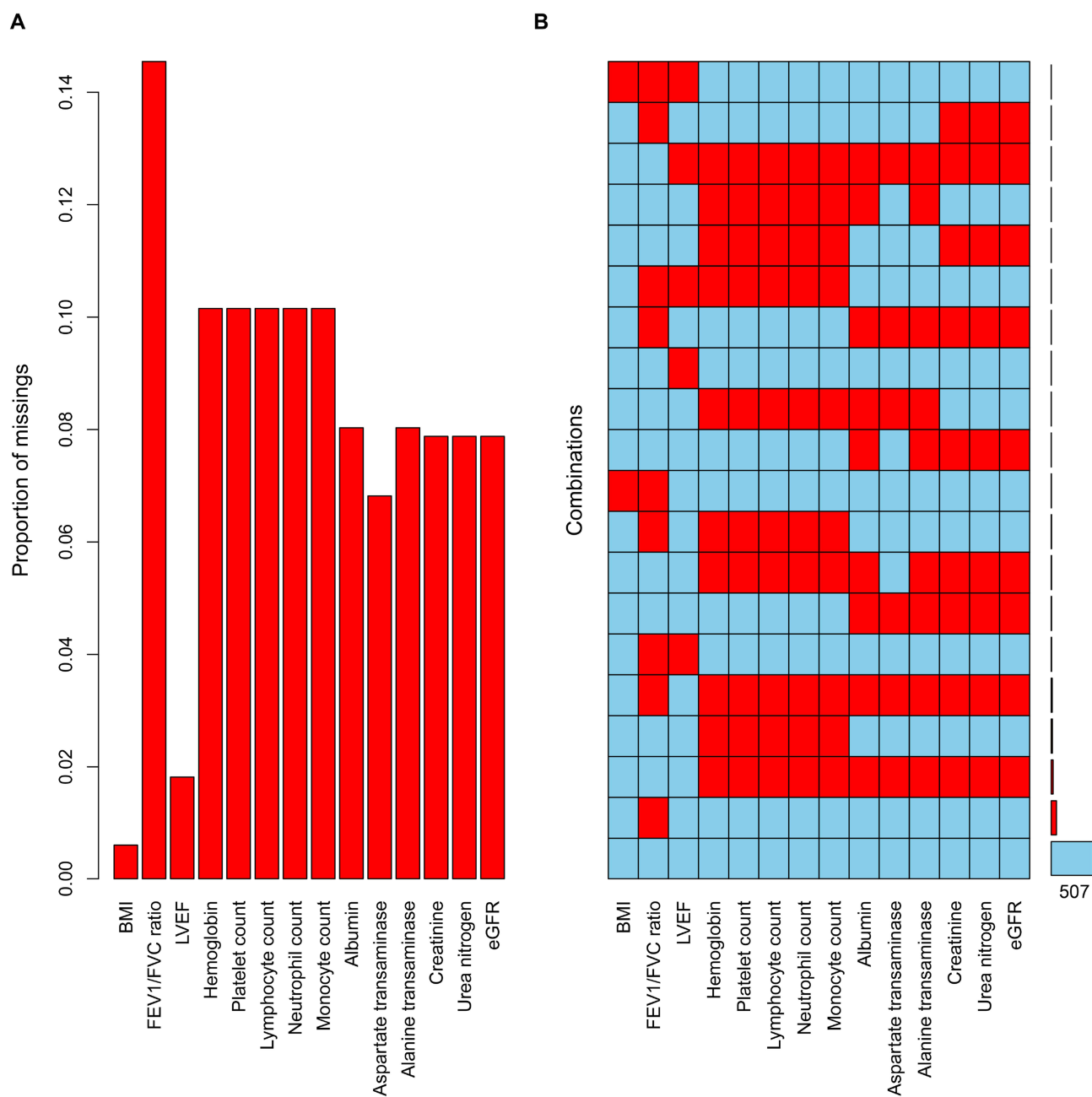


Figure 1 Specific distribution of missing variables. **(A)** Proportion of missing variables. The missing rate varied from 0.6% to 14.5%; **(B)** Quantification of missing values across different combinations of variables. Red squares indicate missing data.

Abbreviations: BMI, body mass index; FEV1/FVC, forced expiratory volume in one second/forced vital capacity; eGFR, estimated glomerular filtration rate.

parameters, with a total of 14 missing indicators (Figure 1). The most conspicuous missing indicator was the FEV1/FVC ratio, with a 14.5% absence rate, while the remaining absent indicators were approximately 10% or less. As shown in Table 1, 375 (56.82%) patients developed PPCs. The median patient age was 68 years, with 57.27% males. The proportion of patients with smoking and drinking history was 29.70% and 23.48%, respectively. Median values for lung function (FEV1/FVC ratio) and heart function (LVEF) were 72.52% and 61%, respectively. The median EuroScore among the entire elderly population was 4 (3, 5). Common comorbidities included coronary artery disease (50.91%), hypertension (45.61%), and diabetes (15.61%). Most patients underwent valve surgery (54.85%), followed by combined coronary artery bypass grafting (CABG) and valve surgery (25.91%).

Table 1 The Characteristics of Patients

Characteristic	Total (n = 660)	Non-PPCs (n = 285)	PPCs (n = 375)	P value
Age, years	68 (66, 70)	68 (66, 70)	68 (66, 71)	0.74
Age ≥75 years	54 (8.18)	21 (7.37)	33 (8.8)	0.506
Male	378 (57.27)	172 (60.35)	206 (54.93)	0.163
BMI ≥28 kg/m ²	54 (8.18)	26 (9.12)	28 (7.47)	0.442
Drinking history	155 (23.48)	76 (26.67)	79 (21.07)	0.093
Smoking history	196 (29.7)	84 (29.47)	112 (29.87)	0.913
FEV1/FVC ratio, %	72.52 (66.37, 77.84)	73.26 (67, 78.3)	71.98 (66.08, 77)	0.108
FEV1/FVC ratio <70%	273 (41.36)	109 (38.25)	164 (43.73)	0.156
LVEF, %	61 (57, 65)	61 (57, 65)	62 (58, 66)	0.133
LVEF <50%	57 (8.64)	21 (7.37)	36 (9.6)	0.312
EuroScore	4 (3, 5)	4 (3, 5)	3 (3, 5)	< 0.001
EuroScore				0.012
≤ 2	125 (18.94)	67 (23.51)	58 (15.47)	
3–5	415 (62.88)	176 (61.75)	239 (63.73)	
≥6	120 (18.18)	42 (14.74)	78 (20.8)	
Hypertension	301 (45.61)	124 (43.51)	177 (47.2)	0.346
Diabetes	103 (15.61)	43 (15.09)	60 (16)	0.749
Coronary artery disease	336 (50.91)	133 (46.67)	203 (54.13)	0.057
Myocardial infarction	32 (4.85)	12 (4.21)	20 (5.33)	0.506
Cerebrovascular disease	43 (6.52)	17 (5.96)	26 (6.93)	0.618
Pulmonary hypertension	21 (3.18)	9 (3.16)	12 (3.2)	0.976
Atrial fibrillation	169 (25.61)	70 (24.56)	99 (26.4)	0.592
Positive inotropic drug use	19 (2.88)	9 (3.16)	10 (2.67)	0.709
Antibiotic use	127 (19.24)	62 (21.75)	65 (17.33)	0.154
Surgical incision				0.077
Median sternotomy	607 (91.97)	256 (89.82)	351 (93.6)	
Minimally invasive	53 (8.03)	29 (10.18)	24 (6.4)	
Type of surgery				< 0.001
CABG	96 (14.55)	52 (18.25)	44 (11.73)	
CABG + Valve	171 (25.91)	53 (18.6)	118 (31.47)	
Valve	362 (54.85)	172 (60.35)	190 (50.67)	
Aorta	31 (4.7)	8 (2.81)	23 (6.13)	
CPB time	110 (85, 137)	108 (84, 129)	112 (86, 150)	0.004
CPB time >150 min	123 (18.64)	31 (10.88)	92 (24.53)	< 0.001
Aortic cross-clamp time	70 (50, 91)	68 (49, 87)	74 (52, 95)	0.026
Aortic cross-clamp time >120 min	54 (8.18)	14 (4.91)	40 (10.67)	0.008
Duration of surgery, min	248 (210, 312.25)	240 (195, 295)	265 (213, 327)	< 0.001
Duration of surgery, min				0.001
<180	59 (8.94)	33 (11.58)	26 (6.93)	
180–240	255 (38.64)	125 (43.86)	130 (34.67)	
>240	346 (52.42)	127 (44.56)	219 (58.4)	
Duration of anesthesia, min	311 (263, 375)	298 (251, 356)	325 (271, 395)	< 0.001
Duration of anesthesia >240 min	554 (83.94)	228 (80)	326 (86.93)	0.016
Blood transfusion	405 (61.36)	159 (55.79)	246 (65.6)	0.01
Use of IABP before extubation	29 (4.39)	2 (0.7)	27 (7.2)	< 0.001
Hemoglobin, g/L	124.60±16.45	125.8±15.42	123.69±17.16	0.102
Anemia	333 (50.45)	144 (50.53)	189 (50.4)	0.974
Platelet count, *10 ⁹ /L	169 (131, 208)	172 (135, 212)	167 (126.5, 204.5)	0.116
Lymphocyte count, *10 ⁹ /L	1.61 (1.28, 2)	1.62 (1.31, 2.03)	1.6 (1.28, 1.96)	0.274
Neutrophil count, *10 ⁹ /L	3.12 (2.54, 4.06)	3.17 (2.5, 4.06)	3.07 (2.57, 4.08)	0.993
Monocyte count, *10 ⁹ /L	0.43 (0.34, 0.56)	0.44 (0.33, 0.56)	0.42 (0.34, 0.56)	0.651

(Continued)

Table 1 (Continued).

Characteristic	Total (n = 660)	Non-PPCs (n = 285)	PPCs (n = 375)	P value
Serum albumin, g/L	39.54±3.60	39.97±3.44	39.21±3.68	0.007
Serum albumin <40 g/L	366 (55.45)	143 (50.18)	223 (59.47)	0.017
Aspartate transaminase, U/L	22 (18, 28)	21 (18, 26)	22 (18, 29)	0.209
Aspartate transaminase >40 U/L	35 (5.3)	14 (4.91)	21 (5.6)	0.696
Alanine transaminase, U/L	19 (14, 28)	18 (14, 28)	19 (14, 28)	0.967
Alanine transaminase >40 U/L	67 (10.15)	36 (12.63)	31 (8.27)	0.066
Serum creatinine, μmol/L	77.8 (66.35, 92.6)	76.3 (65.8, 91.9)	79.1 (67, 93.2)	0.159
Serum creatinine >133 μmol/L	30 (4.55)	11 (3.86)	19 (5.07)	0.461
Urea nitrogen, mmol/L	6.19 (5.16, 7.65)	6.15 (5.21, 7.53)	6.22 (5.14, 7.72)	0.589
Urea nitrogen >7.5 mmol/L	180 (27.27)	73 (25.61)	107 (28.53)	0.404
eGFR, mL/min/1.73m ²	78.14±18.85	80.14±18.40	76.62±19.07	0.017
eGFR <60 mL/min/1.73m ²	121 (18.33)	42 (14.74)	79 (21.07)	0.037

Note: Data are presented as mean (SD) or median (interquartile range) or number of patients (%). Anemia was defined as hemoglobin < 130 g/L for men or < 120 g/L for women.

Abbreviations: BMI, body mass index; FEV1/FVC, forced expiratory volume in one second/forced vital capacity; LVEF, left ventricular ejection fraction; EuroScore, European System for Cardiac Operative Risk Evaluation; CABG, coronary artery bypass grafting; CPB, cardiopulmonary bypass; IABP, intra-aortic balloon pump; eGFR, estimated glomerular filtration rate.

Variables Associated with PPCs

Notably, trends in the association of continuous variables and their conversion to categorical variables with postoperative pulmonary complications were consistent. Univariate analysis revealed statistically significant differences in serum albumin, eGFR, CPB time, aortic cross-clamp time, duration of surgery, duration of anesthesia, type of surgery, blood transfusion, and use of IABP before extubation (Table 1). We incorporated statistically significant categorical variables into the multivariate regression model to facilitate clinical interpretation. In the multivariate model, it was found that the serum albumin level <40 g/L (adjusted odds ratio [OR], 1.43; 95% confidence interval [CI], 1.03–1.98; $P = 0.032$), combined CABG and valve surgery (adjusted OR, 2; 95% CI, 1.14–3.51; $P = 0.016$), aorta-related surgery (adjusted OR, 2.6; 95% CI, 1.01–6.7; $P = 0.047$), CPB time >150 min (adjusted OR, 1.93; 95% CI, 1.01–3.66; $P = 0.046$), blood transfusion (adjusted OR, 1.44; 95% CI, 1.03–2.01; $P = 0.033$), and the use of IABP before extubation (adjusted OR, 7.36; 95% CI, 1.69–32.07; $P = 0.008$) were independently associated with PPCs (Table 2).

Distribution of PPCs

The specific percentages of PPCs are illustrated in Figure 2. Among the various pulmonary complications, pulmonary infection was the most prevalent (28.79%), followed by pleural effusion requiring thoracic drainage (26.36%) and postoperative mechanical ventilation exceeding 48 hours (22.88%). Conversely, ARDS and reintubation were less frequent. Within patients with PPCs, the majority (57.33%) experienced a single pulmonary complication, while 13.87% had three or more PPCs.

Clinical Impact of PPCs

Both hospitalization and postoperative hospitalization durations were significantly longer in patients with PPCs than those without PPCs (33 vs 27, $P < 0.001$; 18 vs 15, $P < 0.001$). Moreover, patients experiencing PPCs had significantly prolonged postoperative ICU stays and mechanical ventilation (5 vs 3, $P < 0.001$; 42 vs 24, $P < 0.001$). Of the 25 recorded deaths, 22 occurred in the PPCs group (22 vs 3, $P = 0.001$). Furthermore, the tracheotomy rate was significantly higher in patients within the PPCs group (8.53% vs 0.35%, $P < 0.001$). Detailed short-term outcomes for patients with PPCs are presented in Table 3.

Table 2 Multivariable Logistic Regression for Predictors of PPCs

Variables	OR	95% CI	P value
EuroScore			
≤ 2	Reference		
3–5	1.4	0.91–2.14	0.126
≥6	1.47	0.82–2.63	0.196
Serum albumin <40 g/L	1.43	1.03–1.98	0.032
eGFR <60mL/min/1.73m ²	1.38	0.89–2.14	0.147
Type of surgery			
CABG	Reference		
CABG + Valve	2	1.14–3.51	0.016
Aorta	2.6	1.01–6.7	0.047
Valve	1.49	0.9–2.44	0.119
CPB time >150 min	1.93	1.01–3.66	0.046
Aortic cross-clamp time >120 min	0.87	0.37–2.06	0.753
Duration of surgery, min			
<180	Reference		
180–240	1.34	0.7–2.54	0.379
>240	1.59	0.77–3.27	0.214
Duration of anesthesia >240 min	1.04	0.61–1.76	0.893
Blood transfusion	1.44	1.03–2.01	0.033
Use of IABP before extubation	7.36	1.69–32.07	0.008

Abbreviations: PPCs, postoperative pulmonary complications; OR, odds ratio; CI, confidence interval; EuroScore, European System for Cardiac Operative Risk Evaluation; eGFR, estimated glomerular filtration rate; CABG, coronary artery bypass grafting; IABP, intra-aortic balloon pump.

Discussion

Our study confirmed that preoperative low serum albumin levels, type of surgery, prolonged CPB duration, blood transfusion, and IABP utilization were independent predictors for elderly patients after CPB. With the increased life

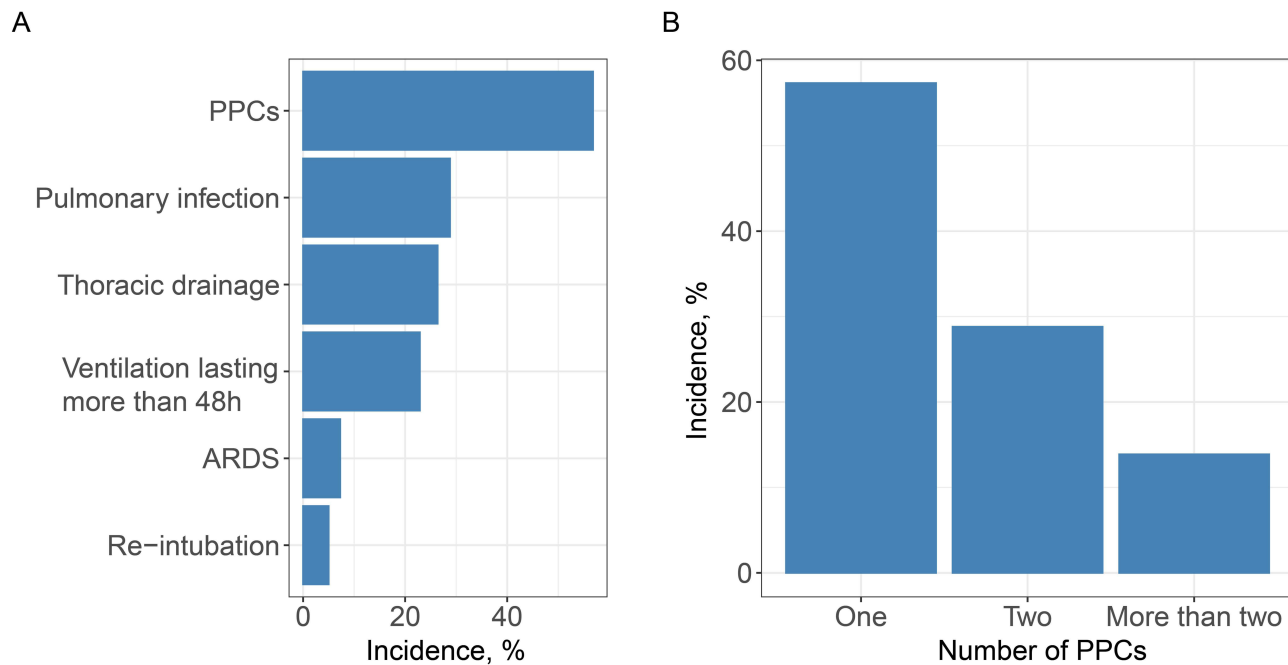


Figure 2 Distribution of PPCs in the Study. **(A)** Proportion of various PPCs: The incidences of individual pulmonary complications, ranked from highest to lowest, were pulmonary infection, pleural effusion requiring thoracic drainage, postoperative mechanical ventilation lasting more than 48 hours, ARDS, and re-intubation. **(B)** Incidence of multiple PPCs in patients. Most patients experienced a single pulmonary complication, with fewer individuals exhibiting various categories of pulmonary complications. **Abbreviations:** PPCs, postoperative pulmonary complications; ARDS, acute respiratory distress syndrome.

Table 3 Comparison of Short-Term Outcomes in Patients with and without PPCs

Variables	Total (n = 660)	Non-PPCs (n = 285)	PPCs (n = 375)	P value
Length of hospitalization, days	30 (24, 38)	27 (22, 33)	33 (26, 42)	< 0.001
Length of postoperative hospitalization, days	16.5 (13, 21)	15 (12, 18)	18 (14, 24)	< 0.001
ICU length of stay, days	4 (3, 5)	3 (2, 4)	5 (4, 7)	< 0.001
Length of postoperative mechanical ventilation, hours	27 (21, 46)	24 (20, 33)	42 (23.5, 63)	< 0.001
Death, %	25 (3.79)	3 (1.05)	22 (5.87)	0.001
Dialysis, %	5 (0.76)	0 (0)	5 (1.33)	0.133
Cerebral infarction, %	2 (0.3)	2 (0.7)	0 (0)	0.186
Tracheotomy, %	33 (5)	1 (0.35)	32 (8.53)	< 0.001

Note: Data are presented as median (interquartile range) or number of patients (%).

Abbreviation: ICU, intensive care unit.

expectancy, there is a growing prevalence of cardiac surgery under CPB among older individuals. Considering the elderly population after CPB is at high risk for PPCs, recognizing these risk factors is crucial for optimizing perioperative management.

The incidence of PPCs varies widely, ranging from 2% to 59%, depending on patient characteristics, PPCs definition, and surgical procedures.¹⁵ In our study, we observed that 56.82% of elderly patients with CPB experienced PPCs, indicating a substantial incidence and enabling the effective identification of specific risk factors. Multivariate analysis revealed that serum albumin levels less than 40g/L, combined CABG and valve surgery, aorta-related surgery, CPB time exceeding 150 min, blood transfusion, and IABP before extubation were associated with an elevated risk of PPCs post-CPB. Consistent with previous research, our findings indicated a significant increase in mortality, ICU stay, and postoperative hospitalization periods for patients with PPCs. Previous studies have reported some risk factors for PPCs after CPB, mainly including age, prolonged CPB time, and preoperative pulmonary hypertension.^{10,16} Our study highlighted different risk factors that fully reflected the distinctiveness of the elderly group and emphasized the necessity of conducting this research. We detailed the incidence of PPCs in older patients undergoing CPB and endeavored to elucidate the potential risk factors and short-term outcomes of PPCs.

Serum albumin, produced and secreted by hepatocytes, serves as an indicator of the body's nutritional status. Furthermore, it functions as a negative acute-phase protein, downregulated during inflammatory states, thereby reflecting both the nutritional status and the inflammatory response and subsequently impacting the patient's postoperative prognosis.¹⁷ With progressive age, serum albumin concentration diminishes at a consistent rate each year.^{18,19} In cardiac surgery, hypoalbuminemia is frequently observed due to surgical loss and significant hemodilution.²⁰ Within our study cohort, 55.45% of patients exhibited albumin concentrations below 40 g/L. Notably, in a prior investigation focusing on off-pump CABG, a preoperative albumin level <40 g/L was independently associated with acute kidney injury.²¹ While several studies in cardiac surgery have explored the relationship between postoperative hypoalbuminemia and adverse outcomes, the consideration of preoperative hypoalbuminemia has been limited.^{22,23} Our emphasis on preoperative albumin levels aimed to identify the optimal opportunity for preventing PPCs. Since low albumin is a modifiable risk factor, optimizing the nutritional status of patients may have a potential in reducing the incidence of PPCs.

CPB-induced local inflammation, systemic inflammatory response syndrome, pulmonary ischemia/reperfusion injury, ventilation arrest, as well as circulating endotoxin collectively increase susceptibility to lung injury.²⁴ As anticipated, our study revealed that patients undergoing more than 150 minutes of CPB time significantly increased the risk of PPCs.

Furthermore, blood transfusion predisposes individuals to pulmonary dysfunction, potentially leading to complications such as transfusion-related acute lung injury and transfusion-associated circulatory overload.²⁵ Studies in cardiac surgery have associated transfusions with adverse outcomes, including mortality, renal failure, pneumonia, and readmission.^{26–28} In a multicenter study involving adult cardiac surgery patients, each additional unit of blood product transfusion was linked to a 7% increased risk of stroke, renal failure, and major infections (deep sternal wound infection, sepsis, and pneumonia).²⁹ Similarly, our study identified a significant positive correlation between blood transfusion and PPCs. IABP, widely used as a mechanical circulatory assist device, often signals compromised cardiac function in

patients. The use of IABP has been subject to some controversy due to its association with higher complication rates.³⁰ A meta-analysis on the prognosis of preoperative IABP implantation in patients undergoing CABG surgery suggested a reduction in the risk of postoperative complications in this specific population.³¹ However, the population in the study was predominantly those with impaired cardiac function, so early support with extracorporeal circulation might positively impact prognosis. Contrarily, our study concluded that using IABP before extubation significantly escalated the risk of PPCs. This observation might be attributed to the absence of patients with preoperative IABP use in our study, where only a small proportion (8.64%) displayed poor preoperative cardiac function (LVEF <50%). Patients requiring intraoperative or postoperative IABP exhibited more critical cardiac conditions and were more likely to develop PPCs.

Our study had several limitations. Firstly, similar to other retrospective studies, inherent selection bias might exist. Secondly, the retrospective nature limited our ability to collect certain parameters, such as frailty and intraoperative mechanical ventilation, which could potentially serve as risk factors for PPCs. Finally, our study was conducted at a single center, potentially limiting its generalizability. Larger prospective trials are necessary to comprehensively validate these findings.

Conclusions

In conclusion, this study identified five simple elements contributing to the risk of PPCs in elderly patients undergoing CPB. PPCs were prevalent in patients after CPB and associated with prolonged mechanical ventilation, extended hospital and ICU stays, higher mortality, and tracheotomy rates. Recognizing and treating the above risk factors may reduce the incidence of PPCs and ultimately improve the prognosis of elderly patients after CPB.

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Disclosure

The authors report no conflicts of interest in this work.

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