Lung-diffusing capacity for carbon monoxide predicts early complications after cardiac surgery

Toshiyuki Kuwata1 · Ikuko Shibasaki1 · Koji Ogata1 · Hironaga Ogawa1 · Yusuke Takei1 · Masahiro Seki1 · Yuriko Kiriya1 · Hirotugu Fukuda1

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Abstract

Purpose Preoperative pulmonary dysfunction has been associated with increased operative mortality and morbidity after cardiac surgery. This study aimed to determine whether values for the diffusing capacity of the lung for carbon monoxide (DLCO) could predict postoperative complications after cardiac surgery.

Methods This study included 408 consecutive patients who underwent cardiac surgery between June 2008 and December 2015. DLCO was routinely determined in all patients. A reduced DLCO was clinically defined as %DLCO < 70%. %DLCO was calculated as DLCO divided by the predicted DLCO. The association between %DLCO and in-hospital mortality was assessed, and independent predictors of complications were identified by a logistic regression analysis.

Results Among the 408 patients, 338 and 70 had %DLCO values of ≥ 70% and < 70%, respectively. Complications were associated with in-hospital mortality (P < 0.001), but not %DLCO (P = 0.275). A multivariate logistic regression analysis with propensity score matching identified reduced DLCO as an independent predictor of complications (OR, 3.270; 95%CI, 1.356–7.882; P = 0.008).

Conclusions %DLCO is a powerful predictor of postoperative complications. The preoperative DLCO values might provide information that can be used to accurately predict the prognosis after cardiac surgery.

Clinical trial registration number UMIN000029985.

Keywords Cardiac surgery · Diffusing capacity of lung for carbon monoxide · Complication

Introduction

Preoperative pulmonary dysfunction in chronic obstructive pulmonary disease (COPD) has been considered to be associated with increased operative mortality and morbidity after cardiac surgery. A careful evaluation of the pulmonary function before and after cardiac surgery demonstrated a significant reduction in lung volume, diffusion capacity, and oxygenation at 2 weeks after surgery, with partial improvement after 4 months [1]. The preoperative identification of patients who are at greater risk of developing complications is important to prevent postoperative complications and obtain a good operative outcome.

The analysis of the diffusing capacity of the lung for carbon monoxide (DLCO) is a clinically useful pulmonary function test (PFT). Unlike other spirometric measurements, DLCO is less influenced by patient effort [2]. DLCO represents the ability of the lung to diffuse carbon monoxide across its membranes and assesses the transfer of gases from the alveoli to red blood cells. The diffusion of O2 depends on the following factors: the alveolar ventilation/capillary perfusion ratio, which establishes the partial pressure gradient of O2 between the alveoli and plasma; the physical characteristics of the alveolar–capillary interface; the capillary blood volume available for gas exchange; the hemoglobin (Hb) concentration; and the reaction rate between O2 and Hb [3, 4]. The diffusion characteristics of the lung are commonly assessed by tests of CO transfer. CO diffuses across the alveoli and binds to Hb with 240-fold greater affinity than O2 [3]. DLCO depends on two resistances arranged in series according to the following equation:

\[ R_{DLCO} = R_{capillary} + R_{alveolar} \]
1/DLCO = 1/D_M + 1/\theta_{\text{CO}} V_C \ [3–5], where D_M is the alveolar–capillary membrane conductance, \( \theta_{\text{CO}} \) is the rate of CO uptake by the whole blood combined with Hb measured in vitro, and V_C is the lung capillary blood volume \[3–5\]. A decline in DLCO can occur as a result of destruction of alveolar structures, distal airway dysfunction, contraction of the pulmonary capillary volume due to ventilation, perfusion abnormalities, and Hb abnormalities.

DLCO is an equally powerful predictor of postoperative complications in patients with and without COPD after lung resection. A previous study suggested that DLCO should be routinely measured during preoperative evaluations, regardless of whether a patient’s spirometric values are abnormal \[2\].

Another study reported that reduced alveolar–capillary membrane conductance is associated with pulmonary congestion \[6\]. Thus, DLCO may be influenced by pulmonary edema and fluid accumulation in the interstitial spaces before and after cardiac surgery. The present study aimed to determine whether DLCO can serve as a predictor of complications arising after cardiac surgery.

**Patients and methods**

**Patients**

The study protocol was approved by the Institutional Review Board of the Dokkyo Medical University. Between June 2008 and December 2015, 2040 patients underwent cardiac surgery at Dokkyo Medical University Hospital. A total of 408 patients in whom preoperative DLCO values were routinely collected within 1 week before scheduled cardiac surgery were included in this study. The attending physician for each patient made the decision to proceed with the PFT, which included measurement of DLCO, based on clinical indications. The exclusion criteria were any emergency or urgent operation, aortic surgery, beating heart surgery, and approaches other than median sternotomy. We reviewed the medical records of the patients, including the demographics, preoperative clinical data, PFT findings, hemodynamic data from cardiac catheterization, and operative and postoperative data.

**DLCO measurement and %DLCO**

We measured DLCO in a single-breath-hold maneuver with the patient seated upright in a chair with their nostrils closed with a clip. The patients then breathed normally and exhaled to residual volume, and then, a carbon monoxide–helium mixture was forcefully inhaled to total lung capacity, and held for 10 s and then exhaled. The patients exhaled to wash out the estimated mechanical and anatomical dead space. Alveolar samples were then collected, and DLCO was calculated from the total volume of the lung, breath-hold duration, and the initial and final alveolar concentrations of CO. The exhaled helium concentration was used to determine a single-breath estimate of the total lung capacity and the initial alveolar concentration of CO. The predicted DLCO was determined from regression equations according to age, height, and sex (predicted DLCO for men, \(15.5 \times \text{body surface area (BSA)} - 0.23 \times \text{age} + 6.8\); predicted DLCO for women, \(15.5 \times \text{BSA} - 0.117 \times \text{age} + 0.5\) \[7\]. %DLCO was calculated by dividing the actual DLCO by the predicted DLCO.

**Surgical technique**

A median sternotomy approach was applied under general anesthesia to all patients. Cardiopulmonary bypass (CPB) was established through the ascending aorta or by right atrial or bicaval cannulation. The myocardium was protected by antegrade and retrograde cardioplegia with intermittent cold-blood cardioplegia and reperfusion with warm-blood cardioplegia. A normothermic temperature was maintained during CPB. The patients were transferred to the intensive care unit immediately after the procedure with ventilator assistance and monitoring.

**Definitions of complications**

Postoperative outcomes were defined according to the Society of Thoracic Surgeons National Database as follows. In-hospital death was defined as the death of a patient due to any cause during hospitalization in the institution, where they underwent cardiac surgery. Stroke was defined as a central neurologic deficit persisting for > 72 h. Wound infection was defined as infection involving subcutaneous tissue, muscle, bone, or the mediastinum, and requiring surgical intervention. Respiratory complications were also included. The incidence of postoperative respiratory complications was scored on an ordinal scale of 1–4, using the operational definitions of postoperative pulmonary complications described by Kroenke et al. \[8\] (Table 1). Clinically significant respiratory complications were defined as one item among grade 3 or 4 complications.

**Statistical analysis**

Continuous variables are expressed as the mean ± standard deviation (SD) and were compared using Student’s t test or the Mann–Whitney test, as appropriate. Nominal variables are expressed as percentages and were analyzed using the \( \chi^2 \) test or Fisher’s exact probability test. All variables with \( P \) values of < 0.20 in the univariate analysis were included in the multivariable analyses. Other clinically relevant
variables, namely, sex, age, body mass index (BMI), and BSA, were adjusted in the multivariable analysis. Independent predictors of postoperative complications after cardiac surgery were identified using a multivariate logistic regression model with the forced entry method. Odds ratios (OR), 95% confidence intervals (95%CI), and $P$ values are reported. To minimize selection bias derived from the retrospective observational study design, propensity score analyses were performed to generate two groups, considering the following covariates: age, sex, BMI, %VC, and hemoglobin. 70 patients with %DLCO < 70% and 67 patients with %DLCO ≥ 70% were matched. A logistic regression analysis for the abovementioned covariates, with nearest-neighbor one-to-one matching, was performed to determine the propensity scores. All statistical tests were two-sided, and $P$ values of < 0.05 were considered to indicate statistical significance. All statistical analyses were performed using the IBM SPSS statistics 24 software program (IBM, Armonk, NY, USA).

### Results

**Patient characteristics and outcomes**

Table 2 summarizes the characteristics of the 408 patients (age, 66.0 ± 10.0 years; male, $n = 295$ [72.3%]), whose data were analyzed in this study. Isolated coronary artery bypass grafting (CABG) was performed for 224 (54.9%) patients, and 184 (45.9%) underwent valve surgery (including concomitant cardiac surgery). Six (1.47%) patients died in hospital due to multi-organ failure ($n = 1$), sudden death ($n = 1$), and sepsis ($n = 4$). Operative complications developed in 91 (22.3%) patients and consisted of gastrointestinal disorder ($n = 3$), stroke ($n = 4$), renal disorder ($n = 5$), cardiac disorder ($n = 7$), wound infection ($n = 19$), and respiratory complications ($n = 71$; Grade 3: $n = 61$, Grade 4: $n = 3$). Figures 1 and 2 show the relationship between patients with all complications or respiratory complications and %DLCO by quartile. The incidence of all complications significantly differed in Q1 (OR, 3.323; 95%CI, 1.472–7.500; $P = 0.005$); the OR for respiratory complications was 3.462 (95%CI, 1.434–8.357; $P = 0.005$). Although a DLco value of < 80% of the predicted value was considered abnormal, according to a previous definition by Steenhuis et al. [9], the incidence of complications differed in Q1 (%DLco < 74.6%). A DLco value of < 70% the predicted value was considered to be the cut-off value. The area under the receiver operating characteristic curve values was 0.625 (95%CI 0.558–0.692) for all complications and 0.632 (95%CI 0.557–0.707) for respiratory complications. The sensitivity and specificity of %DLco, with a cut-off value of 70%, were 0.864 and 0.297, respectively, for all complications (0.861 and 0.324 for respiratory complications).

| Grade | Definition |
|-------|------------|
| 1     | Cough, dry  |
|       | Microatelectasis: abnormal lung findings and temperature $> 37.5$ °C without other documented cause; results of chest radiograph either normal or unavailable |
|       | Dyspnea, not due to other documented cause |
| 2     | Cough, productive, not due to other documented cause  |
|       | Bronchospasm: new wheezing or pre-existent wheezing resulting in change of therapy |
|       | Hypoxemia: arterial–venous gradient $> 29$ and symptoms of dyspnea or wheezing |
|       | Hypercarbia, transient, requiring treatment, such as naloxone or increased manual or mechanical ventilation as an adverse reaction to pulmonary medication |
| 3     | Pleural effusion, resulting in thoracentesis  |
|       | Pneumonia, suspected: radiological evidence without bacteriological confirmation |
|       | Pneumonia, proved: radiological evidence and documentation of pathological organism by Gram stain or culture |
|       | Pneumothorax |
|       | Re-intubation postoperatively or intubation, period of ventilator dependence does not exceed 48 h |
| 4     | Ventilatory failure: postoperative ventilator dependence exceeding 48 h, or re-intubation with subsequent period of ventilator dependence exceeding 48 h |

Table 2 shows the preoperative and perioperative factors of patients with %DLCO of ≥ 70% ($n = 338$) or < 70% ($n = 70$). Significant differences were observed in age (66.5 ± 9.70 vs. 63.8 ± 11.2 years; $P = 0.036$) and sex (female) (86 [25.4%] vs. 27 [38.6%]; $P = 0.025$). There were no significant differences in the risk factors, which included hypertension, hyperlipidemia, history of smoking, BMI, BSA, and HbA1c. Among the clinical and biochemical parameters, significant differences were observed in extracardiac arteriopathy (52 [15.4%] vs. 21 [30.0%]; $P = 0.004$) and Hb (13.1 ± 1.7 vs. 13.8 ± 1.8 mmol/L; $P = 0.001$).

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Table 1 Operational definitions of postoperative pulmonary complications

| Grade | Definition |
|-------|------------|
| 1     | Cough, dry  |
|       | Microatelectasis: abnormal lung findings and temperature $> 37.5$ °C without other documented cause; results of chest radiograph either normal or unavailable |
|       | Dyspnea, not due to other documented cause |
| 2     | Cough, productive, not due to other documented cause  |
|       | Bronchospasm: new wheezing or pre-existent wheezing resulting in change of therapy |
|       | Hypoxemia: arterial–venous gradient $> 29$ and symptoms of dyspnea or wheezing |
|       | Hypercarbia, transient, requiring treatment, such as naloxone or increased manual or mechanical ventilation as an adverse reaction to pulmonary medication |
| 3     | Pleural effusion, resulting in thoracentesis  |
|       | Pneumonia, suspected: radiological evidence without bacteriological confirmation |
|       | Pneumonia, proved: radiological evidence and documentation of pathological organism by Gram stain or culture |
|       | Pneumothorax |
|       | Re-intubation postoperatively or intubation, period of ventilator dependence does not exceed 48 h |
| 4     | Ventilatory failure: postoperative ventilator dependence exceeding 48 h, or re-intubation with subsequent period of ventilator dependence exceeding 48 h |
12.3 ± 1.9 g/dL; *P < 0.001). In terms of the cardiac function, the brain natriuretic peptide (BNP) levels of the two groups were significantly different (193.6 ± 381.3 vs. 265.3 ± 497.1 pg/mL; *P = 0.023), whereas ejection fraction was not (57.7% ± 13.7% vs. 56.0% ± 14.0%; *P = 0.345). Among the factors associated with the respiratory function, %VC was significantly different (95.6 ± 16.3% vs. 89.6 ± 16.5%; *P = 0.005), whereas FEV1.0% was not (72.6 ± 10.6% vs. 72.4 ± 12.6%; *P = 0.878). Among the factors associated with the renal function, the serum creatinine level did not differ to a statistically significant extent (1.3 ± 1.7 vs. 1.3 ± 1.7 mg/dL; *P = 0.306).

CABG was the only operative method for which there was significant difference (193 [57.1%] vs. 31 [44.3%]; *P = 0.050). The operative time (322.5 ± 79.2 vs. 323 ± 85.3 min; *P = 0.350), pump time (144.3 ± 49.9 vs. 152.0 ± 51.5 min; *P = 0.244), and aortic clamp time (105.0 ± 22.6 vs. 110.2 ± 40.5 min; *P = 0.347) did not differ to a statistically significant extent. Furthermore, there was no significant difference in the rate of hospital mortality (4 [1.2%] vs. 2 [2.9%]; *P = 0.275). There were significant differences between the two groups in the rates of all complications (64 [18.9%] vs. 27 [38.6%]; *P < 0.001) and respiratory complications (48 [14.2%] vs. 23 [32.9%]; *P < 0.001).

### Table 2

Demographics and clinical variables stratified by %DLCO risk

|                      | All patients (n = 408) | %DLCO ≥ 70% (n = 338) | %DLCO < 70% (n = 70) | P     |
|----------------------|-----------------------|-----------------------|----------------------|-------|
| Female, n (%)        | 113 (27.7)            | 86 (25.4)             | 27 (38.6)            | 0.025 |
| Age (years)          | 66 ± 10.0             | 66.5 ± 9.7            | 63.8 ± 11.2          | 0.036 |
| BMI (kg/m²)          | 23.6 ± 3.5            | 23.6 ± 3.5            | 23.3 ± 3.4           | 0.412 |
| BSA (m²)             | 1.64 ± 0.19           | 1.64 ± 0.19           | 1.62 ± 0.19          | 0.413 |
| Hypertension, n (%)  | 330 (80.9)            | 276 (81.7)            | 54 (77.1)            | 0.382 |
| Hyperlipidemia, n (%)| 264 (64.7)            | 219 (64.8)            | 45 (64.3)            | 0.936 |
| Smoking, n (%)       | 264 (64.7)            | 213 (63.0)            | 51 (72.9)            | 0.117 |
| Hemoglobin A1C, (%)  | 6.0 (1.0)             | 6.0 (0.9)             | 6.2 (1.3)            | 0.113 |
| NYHA class (I, II), n (%)| 332 (81.4)         | 275 (81.4)            | 57 (81.4)            | 0.382 |
| Recent AMI, n (%)    | 17 (4.2)              | 14 (4.1)              | 3 (4.3)              | 0.956 |
| Atrial fibrillation, n (%)| 79 (19.4)          | 64 (18.9)             | 15 (21.4)            | 0.631 |
| Ex. arteriopathy, n (%)| 73 (17.9)           | 52 (15.4)             | 21 (30.0)            | 0.004 |
| EF (%)               | 57.4 ± 13.7           | 57.7 ± 13.7           | 56.0 ± 14.0          | 0.345 |
| BNP (pg/mL)          | 205.93 ± 403.7        | 193.6 ± 381.3         | 265.3 ± 497.1        | 0.023*|
| %VC (%)              | 94.6 ± 16.3           | 95.6 ± 16.1           | 89.6 ± 16.5          | 0.005 |
| FEV1.0% (%)          | 72.6 ± 10.6           | 72.6 ± 10.1           | 72.4 ± 12.6          | 0.878 |
| PaO2 (mmHg)          | 89.1 ± 13.2           | 89.2 ± 2.9            | 88.5 ± 14.8          | 0.690 |
| PaCO2 (mmHg)         | 39.7 ± 3.9            | 39.8 ± 3.9            | 39.2 ± 4.3           | 0.328 |
| Hemoglobin (g/dL)    | 13.0 ± 1.8            | 13.1 ± 1.7            | 12.3 ± 1.9           | <0.001|
| Creatinine (mg/dL)   | 1.3 ± 1.7             | 1.3 ± 1.7             | 1.3 ± 1.7            | 0.306*|
| Euro score II        | 2.05 ± 1.8            | 1.99 ± 1.7            | 2.34 ± 1.9           | 0.051*|
| STS score            | 2.25 ± 2.77           | 2.21 ± 2.73           | 2.48 ± 2.98          | 0.516*|
| CABG only, n (%)     | 224 (54.9)            | 193 (57.1)            | 31 (44.3)            | 0.050 |
| Operative time (min) | 324.2 ± 80.2          | 322.5 ± 79.2          | 332.3 ± 85.3         | 0.350 |
| Pump time (min)      | 145.7 ± 50.2          | 144.3 ± 49.9          | 152.0 ± 51.5         | 0.244 |
| Aortic clamp time (min)| 105.97 ± 42.3        | 105.0 ± 42.6          | 110.2 ± 40.5         | 0.347 |
| All complications, n (%)| 91 (22.3)           | 64 (18.9)             | 27 (38.6)            | <0.001|
| Resp. complication, n (%)| 71 (17.4)           | 48 (14.2)             | 23 (32.9)            | <0.001|
| Hospital mortality, n (%)| 6 (1.5)              | 4 (1.2)               | 2 (2.9)              | 0.275 |

Continuous data are presented as mean ± SD

BMI body mass index, BNP brain natriuretic peptide, BSA body surface area, CABG coronary artery bypass graft, EF ejection fraction, Ex. arteriopathy extracardiac arteriopathy, FEV1.0% percent predicted forced expiratory volume in 1 s, NYHA New York Heart Association, %VC percent predicted vital capacity, Recent AMI acute myocardial infarction within 3 months, Resp respiratory, STS Society of Thoracic Surgeons, %DLCO percent predicted diffusing capacity of lung for carbon monoxide

*Fisher exact test or Mann–Whitney test

[^1]: Springer
%DLCO as a predictor of complications after cardiac surgery

Table 3 shows the results of the univariate analysis of patients with all complications and those with respiratory complications. Among the preoperative data, significant differences were observed in the rates of %DLCO < 70%, BNP ≥ 100 pg/mL, Hb < 11 g/dL, and the Euro Score II and STS score values of the patients with and without all and those with and without respiratory complications. Among the perioperative factors, significant differences were observed in the operative time, the pump time and the aortic clamp time between the patients with and without complications. A multivariate logistic regression analysis identified BMI (OR, 1.156; 95%CI, 1.039–1.286; P = 0.008), BSA (OR, 0.040; 95%CI, 0.003–0.575; P = 0.018), and a reduced %DLCO (OR, 2.682; 95%CI, 1.449–4.962; P = 0.002) as preoperative factors that were significant independent predictors of all complications. Pump time (OR, 1.016; 95%CI, 1.003–1.030; P = 0.017) as identified as a perioperative factor that was a significant predictor of all complications (Table 4). The multivariate logistic regression analysis identified a reduced %DLCO (OR, 2.833; 95%CI, 1.490–5.398; P = 0.001) and increased HbA1C (OR, 2.284; 95%CI, 1.102–4.733; P = 0.026) as preoperative factors that were significant independent predictors of respiratory complications (Table 5). The propensity score analysis identified a reduced %DLCO as a predictor of all complications and respiratory complications: all complications (OR, 3.270; 95%CI, 1.356–7.882; P = 0.008) and respiratory complications (OR, 3.447; 95%CI, 1.343–8.846; P = 0.010) (Table 6).

Discussion

The principal finding of this study was that the preoperative DLCO was correlated with postoperative complications after cardiac surgery. Others have described significant and prolonged impairment of the pulmonary function after cardiac surgery [1]. Decreased ventilation, pulmonary disease, and reduced alveolar perfusion caused by poor cardiac output and chronic heart failure might also influence DLCO [10]. DLCO is a clinically useful indicator of the lung function, because it assesses gas transfer from the alveoli to the red blood cells. The preoperative DLCO is not routinely measured in patients in most cardiac surgery units. Reduced postoperative capillary filtration due to basal membrane thickening, enhanced alveolar fluid clearance, and increased lymphatic drainage leads to restricted lung spirometry and impaired gas transfer [6]. We hypothesized that the postoperative DLCO might be more decreased than the preoperative DLCO and that this could serve as a predictor of early complications after cardiac surgery. The present study found that more postoperative complications developed among patients with %DLCO of < 70% than among those with %DLCO of > 70%. A previous study also found that patients with stable chronic heart failure had decreased %VC values, in addition to decreased DLCO and D50 values [11]. The present study showed that the %VC values were decreased and the BNP levels were increased in patients with lower DLCO values; however, these patients might have had preoperative chronic heart failure. Thus, %DLCO might be a marker of heart failure.
A previous study suggested that cardiac surgery may also contribute to a greater reduction in DLCO. The mechanism underlying the reduction of DLCO after cardiac surgery is unclear. One hypothesis is that it might reflect pathophysiological changes in the pulmonary microcirculation initiated by CPB, such as a systemic inflammatory response with coagulopathy and altered microvascular permeability [12]. That CPB interferes with pulmonary function has been established. It can induce adverse effects on alveolar stability by activating the complement cascade, sequestering neutrophils in the pulmonary microvascular bed, releasing oxygen-derived free radicals, and changing the composition of alveolar surfactant [13]. The mechanism underlying the diffusion impairment after cardiac surgery could be caused by pulmonary edema and the accumulation of fluid in interstitial spaces, ventilation–perfusion mismatches, or changes in Hb concentrations [14]. A few studies have identified a relationship between DLCO and the outcomes after cardiac surgery. Published data show that a %DL CO value of < 50% the predicted value at the preoperative PFT is an independent risk factor for a > threefold increase in mortality after adjustment for mortality risk estimates [15]. Few patients in the present study had a %DLCO value of < 50%. Thus, our analysis included %DL CO < 70% as an approximation for Q1. The findings of the present study showed that %DLCO < 70% in a preoperative PFT was independently associated with a > 3.3-fold increase in

| Table 3 Demographics of patients and the clinical variables according to complications |
|---------------------------------------------------------------|
| **Continuous data are presented as mean ± SD** |
| **BMI** body mass index, **BNP** brain natriuretic peptide, **BSA** body surface area, **CABG** coronary artery bypass graft, **EF** ejection fraction, **Ex. arteriopathy** extracardiac arteriopathy, **FEV1.0%** percent predicted forced expiratory volume in 1 s, **NYHA** New York Heart Association, **%VC** percent predicted vital capacity, **Recent AMI** acute myocardial infarction within 3 months, **Resp** respiratory, **STS** Society of Thoracic Surgeons, **%DL CO** percent predicted diffusing capacity of lung for carbon monoxide |
| **P** |

| All complications | Respiratory complications |
|-------------------|--------------------------|
| Absent (n = 317) | Present (n = 91) | P | Absent (n = 337) | Present (n = 71) | P |
| Sex, female, n (%) | 85 (26.8) | 28 (30.8) | 0.457 | 89 (26.4) | 24 (33.8) | 0.206 |
| Age ≥ 75 years, n (%) | 62 (19.6) | 20 (22.0) | 0.612 | 65 (19.3) | 17 (23.9) | 0.374 |
| BMI (kg/m²) | 23.6 ± 3.4 | 23.6 ± 3.8 | 0.912 | 23.6 ± 3.4 | 23.4 ± 3.8 | 0.610 |
| BSA (m²) | 1.64 ± 0.2 | 1.61 ± 0.09 | 0.147 | 1.64 ± 0.19 | 1.6 ± 0.19 | 0.069 |
| Hypertension, n (%) | 255 (80.4) | 75 (82.4) | 0.673 | 272 (80.7) | 78 (81.7) | 0.849 |
| Hyperlipidemia, n (%) | 208 (65.6) | 56 (61.5) | 0.473 | 221 (65.6) | 43 (60.6) | 0.442 |
| Smoking, n (%) | 202 (63.7) | 62 (68.1) | 0.438 | 219 (65.0) | 45 (63.4) | 0.797 |
| Hemoglobin A1c ≥ 7%, n (%) | 45 (14.4) | 19 (21.1) | 0.123 | 47 (14.2) | 17 (23.9) | 0.041 |
| NYHA grade > III, n (%) | 54 (17.0) | 22 (24.2) | 0.123 | 58 (17.2) | 18 (25.4) | 0.109 |
| Recent AMI, n (%) | 15 (4.7) | 2 (2.2) | 0.286 | 15 (4.5) | 2 (2.8) | 0.531 |
| Atrial fibrillation, n (%) | 56 (17.7) | 23 (25.3) | 0.105 | 60 (17.8) | 19 (26.8) | 0.083 |
| Ex. arteriopathy, n (%) | 57 (18.0) | 16 (17.6) | 0.930 | 60 (17.8) | 13 (18.3) | 0.920 |
| EF < 40%, n (%) | 35 (11.0) | 13 (14.3) | 0.397 | 38 (11.3) | 10 (14.1) | 0.504 |
| BNP ≥ 100 pg/mL, n (%) | 140 (44.7) | 54 (60.0) | 0.011 | 152 (45.8) | 42 (59.2) | 0.041 |
| %DL CO < 70%, n (%) | 43 (13.6) | 27 (29.7) | <0.001 | 47 (13.9) | 23 (32.4) | <0.001 |
| %VC < 80%, n (%) | 45 (14.2) | 20 (22.0) | 0.074 | 50 (14.8) | 15 (21.1) | 0.188 |
| FEV1.0% ≥ 75%, n (%) | 158 (49.8) | 43 (47.3) | 0.663 | 167 (49.6) | 34 (47.9) | 0.798 |
| PaO2 < 80 mmHg, n (%) | 69 (23.3) | 16 (18.8) | 0.381 | 72 (22.9) | 13 (19.7) | 0.575 |
| PaCO2 ≥ 40 mmHg, n (%) | 147 (49.7) | 39 (45.9) | 0.539 | 157 (49.8) | 29 (43.9) | 0.383 |
| Hemoglobin, < 11 g/dL, n (%) | 36 (11.4) | 19 (20.9) | 0.019 | 40 (11.9) | 15 (21.1) | 0.038 |
| Creatinine ≥ 2.0 mg/dL, n (%) | 23 (7.3) | 9 (9.9) | 0.410 | 26 (7.7) | 6 (8.5) | 0.834 |
| Euro Score II | 1.90 ± 1.58 | 2.59 ± 2.34 | 0.001* | 1.91 ± 1.57 | 2.72 ± 2.53 | 0.003* |
| STS score | 2.04 ± 2.51 | 3.01 ± 3.44 | 0.002* | 2.09 ± 2.57 | 3.06 ± 3.49 | 0.006* |
| CABG alone, n (%) | 178 (56.2) | 46 (50.5) | 0.344 | 188 (55.8) | 36 (50.7) | 0.434 |
| Operative time (min) | 318.7 ± 79.8 | 343.1 ± 79.4 | 0.010 | 320.5 ± 79.6 | 341.5 ± 81.6 | 0.045 |
| Pump time (min) | 140.7 ± 45.2 | 163 ± 61.9 | 0.002 | 142.3 ± 45.7 | 161.7 ± 65.9 | 0.020 |
| Aortic clamp time (min) | 103 ± 38.8 | 116.2 ± 51.4 | 0.025 | 104 ± 39.4 | 115.2 ± 53.1 | 0.094 |

Continuous data are presented as mean ± SD

BMI body mass index, BNP brain natriuretic peptide, BSA body surface area, CABG coronary artery bypass graft, EF ejection fraction, Ex. arteriopathy extracardiac arteriopathy, FEV1.0% percent predicted forced expiratory volume in 1 s, NYHA New York Heart Association, %VC percent predicted vital capacity, Recent AMI acute myocardial infarction within 3 months, Resp respiratory, STS Society of Thoracic Surgeons, %DL CO percent predicted diffusing capacity of lung for carbon monoxide

*Fisher exact test or Mann–Whitney test
Postoperative respiratory complications continue to affect patient morbidity and mortality, length of hospital stay, and overall resource utilization, despite advances in preoperative, intraoperative, and postoperative care [16–18]. Respiratory muscle dysfunction due to surgery can lead to a reduced vital capacity, tidal volume, and total lung capacity [19]. This could cause atelectasis in the basal lung segments

| Table 4 Univariate and multivariate analyses of the predictors of all complications |
|-----------------|-----------------|-----------------|-----------------|-----------------|
|                  | Univariate analysis | Multivariate analysis |
|                  | OR (95%CI) | P     | OR (95%CI) | P     |
| Sex (female)     | 1.213 (0.729–2.020) | 0.458 | 0.463 (0.199–1.076) | 0.074 |
| Age (≥ 75 years) | 1.159 (0.656–2.046) | 0.612 | 0.745 (0.354–1.566) | 0.438 |
| BMI (kg/m²)      | 1.004 (0.939–1.073) | 0.917 | 1.156 (1.039–1.286) | 0.008 |
| BSA (m²²)        | 1.034 (0.933–1.147) | 0.148 | 0.040 (0.003–0.575) | 0.018 |
| Hemoglobin A1c (≥ 7%) | 1.539 (0.859–2.758) | 0.147 | 1.744 (0.872–3.486) | 0.116 |
| NYHA class (III, IV) | 0.594 (0.878–2.743) | 0.126 | 1.520 (0.794–2.909) | 0.206 |
| Atrial fibrillation | 1.576 (0.906–2.743) | 0.107 | 1.338 (0.660–2.714) | 0.420 |
| BNP (≥ 100 pg/mL) | 1.854 (1.150–2.986) | 0.011 | 1.091 (0.614–1.940) | 0.767 |
| %DLCO (<70%)     | 2.688 (1.547–4.673) | <0.001 | 2.682 (1.449–4.962) | 0.002 |
| %VC (<80%)       | 1.703 (0.946–3.065) | 0.076 | 1.243 (0.620–2.491) | 0.540 |
| Hemoglobin (<11 g/dL) | 2.060 (1.116–3.803) | 0.021 | 1.306 (0.623–2.735) | 0.479 |
| Euro score II    | 1.204 (1.069–1.056) | 0.002 | 1.028 (0.857–1.233) | 0.763 |
| STS score        | 1.857 (1.150–2.986) | 0.011 | 1.091 (0.614–1.940) | 0.767 |
| Operative time (min) | 1.004 (1.001–1.006) | 0.012 | 0.999 (0.995–1.004) | 0.752 |
| Pump time (min)  | 1.009 (1.004–1.013) | <0.001 | 1.016 (1.003–1.030) | 0.017 |
| Aortic clamp time (min) | 1.007 (1.002–1.012) | 0.01 | 0.988 (0.975–1.002) | 0.085 |

| Table 5 Univariate and multivariate analyses of predictors of respiratory complications |
|-----------------|-----------------|-----------------|-----------------|-----------------|
|                  | Univariate analysis | Multivariate analysis |
|                  | OR (95%CI) | P     | OR (95%CI) | P     |
| Sex (female)     | 1.423 (0.822–2.462) | 0.207 | 0.587 (0.239–1.440) | 0.245 |
| Age (≥ 75 years) | 1.317 (0.717–2.421) | 0.375 | 0.942 (0.429–2.068) | 0.882 |
| BMI (kg/m²)      | 1.002 (0.591–1.77) | 0.941 | 1.099 (0.979–1.233) | 0.108 |
| BSA (m²²)        | 0.96 9 (0.070–1.109) | 0.070 | 0.062 (0.003–1.096) | 0.058 |
| HbA1c (≥7%)      | 1.910 (1.020–3.571) | 0.043 | 2.284 (1.102–4.733) | 0.026 |
| NYHA class (III, IV) | 1.634 (0.892–2.991) | 0.112 | 1.512 (0.751–3.261) | 0.246 |
| Atrial fibrillation | 1.687 (0.930–3.058) | 0.085 | 1.516 (0.705–3.261) | 0.287 |
| BNP (≥ 100 pg/mL) | 1.720 (1.020–2.885) | 0.042 | 0.962 (0.514–1.802) | 0.904 |
| %DLCO (<70%)     | 2.960 (1.647–5.306) | <0.001 | 2.833 (1.490–5.388) | 0.001 |
| %VC (<80%)       | 1.537 (0.807–2.928) | 0.191 | 1.022 (0.475–2.196) | 0.956 |
| Hemoglobin (<11 g/dL) | 1.989 (1.029–3.842) | 0.041 | 1.356 (0.621–2.963) | 0.445 |
| Euro score II    | 1.226 (1.084–1.088) | 0.001 | 1.059 (0.876–1.281) | 0.553 |
| STS score        | 1.106 (1.024–1.195) | 0.011 | 1.044 (0.922–1.182) | 0.498 |
| Operative time (min) | 1.003 (1.000–1.006) | 0.047 | 0.999 (0.994–1.004) | 0.703 |
| Pump time (min)  | 1.007 (1.002–1.032) | 0.004 | 1.013 (0.999–1.028) | 0.066 |
| Aortic clamp time (min) | 1.006 (1.000–1.012) | 0.043 | 0.990 (0.976–1.004) | 0.168 |

OR odds ratio, CI confidence interval, BMI body mass index, BNP brain natriuretic peptide, BSA body surface area, NYHA New York Heart Association, %VC percent predicted vital capacity, STS Society of Thoracic Surgeons, %DLCO percent predicted diffusing capacity of lung for carbon monoxide.
and decrease the functional residual capacity, which affects pulmonary gas exchange properties by increasing ventilation/perfusion mismatches. Thus, \( DLCO \) might also decrease after surgery. Preoperative and postoperative chest physical therapy has significantly reduced the number of patients who develop atelectasis, but it does not significantly benefit patients who develop respiratory complications due to infection [20]. Improving the preoperative respiratory status of these patients via the fine adjustment of medication therapy and strict physiotherapeutic control seems important. Preoperative short-term pulmonary rehabilitation for such patients improves the pulmonary function and reduces the incidence of atelectasis, consolidation, and pneumothorax [16]. Preoperative physical therapy with inspiratory muscle training for at least 2 \( \text{weeks} \) reduced the incidence of postoperative pulmonary complications by 50% [18]. Although the present study did not uncover evidence as to whether surgical outcomes would improve with preoperative short-term pulmonary rehabilitation, determining the correct timing of surgery is also important for avoiding respiratory decompensation.

The present study is associated with several limitations. Although all data were prospectively recorded, this was a retrospective, single-institute study. The retrospective design is susceptible to various sources of bias, which might have not been identified or controlled. The preoperative PFTs were performed according to requests from clinicians, who were not blinded to the results of the PFT. Thus, the possibility that patient management might have been affected by the PFT results cannot be excluded.

In conclusion, the \( \%DLCO \) seems to be a powerful predictor of postoperative complications. To the best of our knowledge, this is one of the few studies to assess whether \( DLCO \) is a potential risk factor for adverse outcomes of patients after cardiac surgery. Preoperative \( DLCO \) values might provide more accurate prognostic information about outcomes after cardiac surgery. Preoperative PFT findings might provide clinicians with more accurate risk profiles as well as additional prognostic information. Thus, pulmonary function testing, including measurement of \( DLCO \), should be a routine component of preoperative evaluations.

### Table 6

|                      | All complications | Respiratory complications |
|----------------------|-------------------|--------------------------|
|                      | \( OR \) (95% CI) | \( P \)                  | \( OR \) (95% CI) | \( P \) |
| BSA (m\(^2\))       | 0.446 (0.040–4.943) | 0.511 | 0.273 (0.021–3.504) | 0.319 |
| HbA1c (≥ 7%)         | 0.577 (0.149–2.241) | 0.427 | 0.959 (0.245–3.763) | 0.953 |
| NYHA class (III,IV)  | 2.416 (0.797–7.322) | 0.119 | 1.965 (0.616–6.268) | 0.254 |
| Atrial fibrillation  | 1.977 (0.650–6.136) | 0.227 | 1.547 (0.486–4.923) | 0.460 |
| BNP (≥ 100 pg/mL)    | 0.760 (0.296–1.954) | 0.569 | 0.818 (0.302–2.213) | 0.692 |
| \( %DLCO < 70\% \)  | 3.270 (1.356–7.882) | 0.008 | 3.447 (1.343–8.846) | 0.010 |
| Euro score II        | 1.068 (0.783–1.455) | 0.678 | 1.174 (0.853–1.615) | 0.325 |
| STS score            | 1.050 (0.882–1.249) | 0.586 | 0.968 (0.800–1.172) | 0.740 |
| Operative time (min) | 1.005 (0.997–1.013) | 0.212 | 1.003 (0.995–1.012) | 0.424 |
| Pump time (min)      | 1.002 (0.981–1.024) | 0.828 | 1.003 (0.980–1.026) | 0.818 |
| Aorta clamp time (min)| 1.001 (0.978–1.024) | 0.945 | 1.004 (0.981–1.029) | 0.711 |

Propensity scores were calculated by age, sex, BMI, \%VC and hemoglobin, and 70 patients with \( %DLCO < 70\% \) and 67 patients with \( %DLCO \geq 70\% \) were matched

\( OR \) odds ratio, \( CI \) confidence interval, \( BMI \) body mass index, \( BSA \) body surface area, \( NYHA \) New York Heart Association, \%VC percent predicted vital capacity, \( STS \) Society of Thoracic Surgeons, \( %DLCO \) percent predicted diffusing capacity of lung for carbon monoxide.
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