Chronic obstructive pulmonary disease severity influences outcomes after off-pump coronary artery bypass

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ABSTRACT

Objective: To analyze the impact and severity of chronic obstructive pulmonary disease (COPD) on pulmonary function and postoperative clinical outcome based on the Global Initiative for Obstructive Lung Disease criteria in patients undergoing off-pump coronary artery bypass grafting (CABG).

Methods: Patients were allocated into 3 groups according to presence and severity of COPD: no or mild COPD ($n = 144$); moderate COPD ($n = 77$); and severe COPD ($n = 30$). Spirometry values were obtained preoperatively and on postoperative days (PODs) 2 and 5. The incidences of pneumonia and reintubation, time of mechanical ventilation, and length of postoperative hospital stay were recorded.

Results: Significant impairment in pulmonary function was observed in all groups on PODs 2 and 5 ($P < .001$). However, postoperative pulmonary dysfunction was significantly higher in the moderate and severe COPD groups compared with the no or mild COPD group ($P < .05$). On multivariable analysis, severe COPD was associated with an elevated risk for composite outcomes (odds ratio, 1.37; 95% confidence interval, 1.20-1.57; $P < .001$). A preoperative forced expiratory volume in 1 second (FEV_1) $< 50\%$ of the predicted value was associated with poor outcome. A significant negative correlation was found between FEV_1 at POD 5 and postoperative length of stay ($r = -0.5$; $P < .001$).

Conclusions: More severe COPD was associated with greater impairment in pulmonary function and worse clinical outcomes after off-pump CABG surgery. A preoperative $FEV_1 < 50\%$ of predicted value appears to be an important predictor of postoperative complications. (J Thorac Cardiovasc Surg 2018;156:1554-61)

Optimal cutoff point that maximizes the optimal sensitivity and specificity.

Central Message

Chronic obstructive pulmonary disease severity and preoperative forced expiratory volume in 1 second $< 60\%$ are important predictors of poor outcomes after off-pump coronary artery bypass.

Perspective

Chronic obstructive pulmonary disease (COPD) severity is poorly graded before cardiac surgery, which leads to underestimated preoperative risks. The GOLD criteria take into account spirometric values to classify COPD, and collectively appear to provide a useful tool for determining preoperative risk in patients with COPD undergoing off-pump coronary artery bypass.

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Chronic obstructive pulmonary disease (COPD) is closely linked to coronary artery disease, due to a common risk factor.¹ In the past few years, coronary artery bypass grafting (CABG) has been more routinely performed in high-risk patients, and has proved to be an effective therapeutic option for coronary artery disease.¹⁻³ Despite the positive impact of surgery on quality of life and survival,^{4,5} COPD is

Scanning this QR code will take you to a supplemental video for the article.

Abbreviations and Acronyms

CABG	= coronary artery bypass grafting
COPD	= chronic obstructive pulmonary disease
CPB	= cardiopulmonary bypass
FEV ₁	= forced expiratory volume in 1 second
FVC	= forced vital capacity
GOLD	= Global Initiative for Obstructive Lung Disease
LITA	= left internal thoracic artery
LOS	= length of stay
LVEF	= left ventricular ejection fraction
MARSpline	= multivariate adaptive regression spline
OPCAB	= off-pump coronary artery bypass
POD	= postoperative day

associated with poor prognosis in patients undergoing CABG.⁶ According to EuroSCORE II, COPD is an independent predictor of perioperative mortality.⁷ However, this score does not take disease severity into account, which can lead to a misclassification of preoperative risk. It is possible that the perioperative risk differs among patients across the COPD spectrum (ie, from mild to severe disease).

Regardless of baseline pulmonary function, respiratory mechanics and gas exchange are strongly affected after CABG, increasing the risks of postoperative pulmonary complications.⁸⁻¹⁰ These risks can be further augmented in patients with COPD, in whom the intrinsic and exacerbated inflammatory response may be potentiated by cardiopulmonary bypass (CPB) and other related technical factors. Several previous studies have confirmed the negative influence of severe COPD during the postoperative period in patients undergoing on-pump CABG, as well as its association with higher short- and long-term mortality.^{1,6,11,12} Nevertheless, these results remain controversial due to the heterogeneity of clinical and spirometric variables used to define COPD, which is often diagnosed on an empirical basis without pulmonary function testing.¹³ Moreover, to date no study has clarified the influence of disease severity on pulmonary function and clinical outcomes after CABG, regardless of the use of CPB. Given these gaps in the literature, further investigation is warranted.

The aim of the present investigation was to analyze the impact and severity of COPD on pulmonary function and postoperative clinical outcomes based on the Global Initiative for Obstructive Lung Disease (GOLD) criteria¹⁴ in patients undergoing off-pump CABG (OPCAB).

METHODS

This prospective cohort study was performed at Pirajussara and Sao Paulo Hospitals of the Federal University of Sao Paulo after approval by

the institutional Ethics Committee. All patients provided written voluntary informed consent.

Study Population

Patients undergoing OPCAB were evaluated for participation in this study. Inclusion criteria were age 35 to 75 years, coronary artery disease confirmed by coronary angiography, and elective surgery. Patients who had undergone emergency surgery, required on-pump conversion or bilateral pleurotomy, had a diagnosis of restrictive lung disease, or were unable to perform spirometry were excluded from the study. In terms of baseline clinical characteristics, current smokers were defined according to the National Health Interview Survey¹⁵ as adults who smoked at least 100 cigarettes during their lifetime and reported smoking every day or on some days.

A total of 251 patients were allocated into 3 groups according to the presence and severity of COPD: no or mild COPD group (n = 144), moderate COPD group (n = 77), and severe COPD group (n = 30) (Table 1).

Pulmonary Function Assessment

Forced vital capacity (FVC) and forced expiratory volume in 1 second (FEV₁) were evaluated at the bedside using a portable spirometer (Spirobank G; Medical International Research, Rome, Italy), according to American Thoracic Society standards.¹⁶ Pulmonary function testing was carried out preoperatively and on postoperative days (PODs) 2 and 5 by the same evaluator. The severity of COPD was defined according to the GOLD criteria.¹⁴

Surgical Procedure

Anesthesia was induced in a routine protocol with etomidate and midazolam and maintained with sufentanil and isoflurane (0.5%-1%). The OPCAB surgery was carried out through a median sternotomy, using the left internal thoracic artery (LITA) complemented with additional saphenous vein grafts. The LITA was harvested using a skeletonized technique. Meticulous care is routinely taken to preserve the integrity of the pleura during LITA harvesting. In all cases when the pleural cavity was opened incidentally, a soft tubular pleural drain was inserted and positioned in the left costophrenic sinus and exteriorized at the subxyphoid region or at the sixth intercostal space. In all patients, a straight mediastinal drain was placed as well.

In our institution, OPCAB is performed as follows. After provision of systemic heparinization to achieve an activated clotting time of >250 seconds, occlusion of the coronary artery was accomplished using a proximal soft silicone snare. Distal anastomoses were accomplished with a 7-0 running polypropylene suture. The vein top ends were attached to the ascending aorta using side-bite clamping. An Octopus 3 suction stabilizer (Medtronic, Minneapolis, Minn) was used in all cases (Video 1).

Postoperative Management

After surgery, all patients were transferred to the cardiac intensive care unit. Mechanical ventilation settings were adjusted at 12 to 14 breaths per minute, with a fraction of inspired oxygen level necessary to maintain arterial oxygen saturation, a positive end-expiratory pressure of 5 cm H₂O, and pressure support to maintain a tidal volume of 8 mL/kg of predicted body weight. The same analgesic protocol was administered during the first 5 postoperative days (tramadol 100 mg/day), and all patients received the same rehabilitation protocol. Rescue analgesia was supplemented in patients with a pain score of ≥ 4 on a visual analog scale of 0 to 10.

Clinical Outcomes

The duration of mechanical ventilation, postoperative hospital length of stay (LOS), and incidence of pneumonia were recorded. Hospital LOS was defined as the time from operation to hospital discharge. Prolonged mechanical ventilation was defined as the need for respiratory support for

TABLE 1. COPD classification according to the GOLD standard

Stage	Spirometric values
I: no or mild COPD	FEV ₁ /FVC <70% and FEV ₁ ≥80%
II: moderate COPD	FEV ₁ /FVC <70% and 50% ≤ FEV ₁ <80%
III: severe COPD	FEV ₁ /FVC <70% and 30% ≤ FEV ₁ <50%

COPD, Chronic obstructive pulmonary disease; FEV₁, forced expiratory volume in 1 second; FVC, forced vital capacity.

>24 hours.¹⁷ Prolonged LOS was defined as a hospital LOS >14 days.¹⁸ Pneumonia was defined by the presence on chest radiographs of new, persistent pulmonary infiltrates not otherwise explained, in combination with at least 2 of the following criteria: body temperature >38°C, leukocytosis (>10,000 cells/mm³), and purulent respiratory secretions.¹⁹ The main endpoint was respiratory outcomes, composed of reintubation, pneumonia, and prolonged mechanical ventilation.

Statistical Analysis

The Kolmogorov–Smirnov test was used to verify the normality of data distribution. Categorical data were recorded as absolute (number) and relative (percentage) frequencies and analyzed using the χ^2 test or Fisher's exact test. Continuous variables were recorded as mean $\pm$ standard deviation. The groups were compared using analysis of variance with Tukey's post hoc test. Pairwise comparisons were used when multiple comparisons yielded a significant difference ($P < .05$). The Pearson correlation coefficient was calculated for evaluating the association between POD 5 and FEV₁. A logistic regression model was used to assess the impact of different COPD stages on postoperative complications, adjusting for left ventricular ejection fraction (LVEF), body mass index, age, sex, hypertension, diabetes, dyslipidemia, and smoking. Multivariate adaptive regression splines (MARSplines) analysis was performed to evaluate the prognostic performance of FEV₁ with regard to respiratory outcomes. The cutoff value was attained as the point corresponding to better sensitivity and specificity. A P value <.05 was used to define statistical significance for all tests.

RESULTS

Over the study period, 327 patients were deemed eligible for the study, of whom 286 were allocated into 3 groups, and 251 completed the analysis. A flowchart indicating the progression of patients throughout the study is shown in Figure 1. Baseline clinical and demographic characteristics of all groups are summarized in Table 2. According to our findings, greater COPD severity was associated with a lower LVEF compared with no or mild COPD (0.46 ± 0.05 vs 0.59 ± 0.10 ; $P < .001$) and moderate COPD (0.46 ± 0.05 vs 0.58 ± 0.07 ; $P < .01$) (Table 2).

Significantly impaired FVC and FEV₁ was observed in all groups on PODs 2 and 5 compared with preoperative data ($P < .001$). However, FVC and FEV₁ on PODs 2 and 5 were significantly lower in the moderate COPD and severe COPD groups compared with the no or mild COPD group ($P < .05$). Impairment was significantly greater in the severe COPD group compared with the moderate COPD group (Table 3).

The incidences of reintubation, pneumonia, prolonged mechanical ventilation and increased LOS were higher in

VIDEO 1. Off-pump coronary artery bypass grafting using bilateral internal thoracic arteries (ITAs), with the left ITA anastomosed to the left anterior descending coronary artery and the in situ right ITA routed through the transverse sinus to revascularize the obtuse marginal artery. Video available at: [https://www.jtcvs.org/article/S0022-5223\(18\)31231-5/fulltext](https://www.jtcvs.org/article/S0022-5223(18)31231-5/fulltext).

the severe COPD group compared with the moderate COPD and no or mild COPD groups ($P < .05$). The moderate COPD group had worse outcomes compared with the no or mild COPD group, with the exception of prolonged mechanical ventilation, for which no significant difference was found (Table 4).

In the multivariable analysis for adjusted odds ratio (OR), moderate and severe COPD were significantly associated with greater risk for respiratory outcomes, especially in severe COPD (OR, 1.13; 95% CI 1.05-1.23; $P = .002$ and OR, 1.37; 95% CI, 1.20-1.57; $P < .001$; respectively).

MARSplines analysis demonstrated an optimal cutoff value of 50% of predicted FEV₁ for respiratory outcomes (Table 5 and Figure 2). A significant negative correlation was found between FEV₁ at POD 5 and postoperative hospital LOS ($r = -0.50$; $P < .001$).

FIGURE 1. Flowchart of progression of patients. *COPD*, Chronic obstructive pulmonary disease.

DISCUSSION

The current study revealed that the presence and severity of COPD, based on GOLD criteria, was associated with greater impairment in pulmonary function and worse clinical outcomes in patients undergoing OPCAB. In addition, preoperative FEV₁ <50% seems to be an important predictor for poor outcomes.

Few studies have evaluated the lung function in COPD patients and their influence during the perioperative period of CABG. To our knowledge, this is the first prospective study evaluating preoperative pulmonary function, based on GOLD definitions and the influence of COPD severity on pulmonary function and clinical outcomes after OPCAB.

Pulmonary function is strongly affected after heart surgery, owing to inherent factors associated with surgical procedures. The use of general anesthesia and median sternotomy results in decreased lung compliance and increased respiratory system resistance, inducing postoperative lung dysfunction.^{8,9,20,21} Pulmonary dysfunction is more pronounced when LITA is used, especially if associated with pleura

opening with a consequent need for intercostal pleural drainage, further damaging lung function compared with maintenance of an intact pleura.¹⁰ Furthermore, on-pump CABG also elicits a greater degree of lung dysfunction in the early postoperative period compared with OPCAB, owing to the consequent inflammatory response^{22,23} Despite the outcomes of the CORONARY trial, in which no differences between on-pump and off-pump surgery were seen in the rate of the composite outcome, the impact of pulmonary function and COPD has not been assessed and reported²⁴ Evidence suggests that high-risk patients may benefit from avoiding the deleterious effects of CPB.^{25,26} In a retrospective analysis, Lizak and colleagues²⁷ found better outcomes in patients with COPD undergoing OPCAB compared with those undergoing conventional CABG.

In addition to surgical factors, pre-existing conditions, such as COPD, may potentiate the effects of surgery on pulmonary function and postoperative outcomes. Recent studies have demonstrated that CABG has a positive impact on quality of life in patients with concomitant

TABLE 2. Preoperative and intraoperative clinical and demographic characteristics

Characteristic	No or mild COPD (n = 144)	Moderate COPD (n = 77)	Severe COPD (n = 30)
Age, y, mean $\pm$ SD	59.7 $\pm$ 10	61 $\pm$ 10	63 $\pm$ 11
Sex, n (%)			
Male	122 (84.7)	67 (87.0)	25 (83.0)
Female	22 (15.3)	10 (13.0)	05 (17.0)
LVEF, mean $\pm$ SD	0.59 $\pm$ 0.10	0.58 $\pm$ 0.07*	0.46 $\pm$ 0.05*,†
Comorbidities, n (%)			
LVEF <0.45	15 (10.4)	9 (11.6)*	14 (46.6)*,†
Current smoker	36 (25.0)	34 (44.0)	12 (42.0)
Hypertension	93 (64.5)	52 (67.5)	18 (60.0)
Diabetes	43 (29.8)	25 (32.4)	8 (26.7)
Hypercholesterolemia	87 (60.4)	48 (62.3)	20 (66.6)
Pulmonary function, mean $\pm$ SD			
FVC, L	3.5 $\pm$ 0.7	3.0 $\pm$ 0.4	3.5 $\pm$ 0.5
%pred	88 $\pm$ 13	80 $\pm$ 13	90 $\pm$ 11
FEV ₁ , L	2.8 $\pm$ 0.6	1.8 $\pm$ 0.3*	1.3 $\pm$ 0.3*,†
%pred	89.2 $\pm$ 14.4	59.7 $\pm$ 7.4	42.7 $\pm$ 7.0
FEV ₁ /FVC	81 $\pm$ 8	60 $\pm$ 7*	39 $\pm$ 9*,†
EuroSCORE, mean $\pm$ SD	3.2 $\pm$ 1.8	3.7 $\pm$ 2.0	4.1 $\pm$ 3.1
Pleural drain site, n (%)			
Intercostal	55 (38)	28 (36)	12 (40)
Subxyphoid	89 (62)	49 (64)	18 (60)
Duration of surgery, min, mean $\pm$ SD	296 $\pm$ 22	309 $\pm$ 19	307 $\pm$ 21
Grafts per patient, n, mean $\pm$ SD	2.1 $\pm$ 0.7	2.3 $\pm$ 0.8	2.2 $\pm$ 0.4

COPD, Chronic obstructive pulmonary disease; SD, standard deviation; LVEF, left ventricular ejection fraction; FVC, forced vital capacity; FEV₁, forced expiratory volume in 1 second; %pred, percentage of predicted; SD, standard deviation. * P < .001 versus no or mild COPD. † P < .01 versus moderate COPD.

COPD.⁵ According to EuroSCORE II⁷ and Syntax II score,²⁸ COPD is an independent risk factor for morbidity and mortality postsurgery and is associated with poor prognosis.^{1,6,11,12} However, these scores do not take into account disease severity, and it is possible that perioperative risk differs according to the severity of COPD (ie, from mild to moderate or severe). Few studies used spirometric tests before cardiac surgery in COPD patients, and thus particularly novel aspects of our study are the use of systematic perioperative spirometry evaluation, use of the GOLD criteria, and evaluation of the influence of COPD severity on spirometric values and clinical outcomes.

In the present study, regardless of preoperative pulmonary function or COPD severity, all groups presented with

significantly impaired FVC and FEV₁ at PODs 2 and 5 compared with preoperative values. These results are similar to those reported in previous studies.^{8-10,19} However, postoperative spirometric values were significantly lower in the moderate and severe COPD groups compared with the no or mild COPD group, and the severe COPD group exhibited significantly greater postoperative pulmonary dysfunction compared with the moderate COPD group.

The evidence indicates that a greater degree of pulmonary dysfunction increases the risk of postoperative complications. Our results are consistent with previous studies^{19,21,27} showing that patients with advanced-stage COPD exhibited greater pulmonary dysfunction and poorer outcomes following OPCAB. These results are supported

TABLE 3. Pulmonary function values on PODs 2 and 5

Parameter	POD 2			POD 5		
	No or mild COPD (n = 144)	Moderate COPD (n = 77)	Severe COPD (n = 30)	No or mild COPD (n = 144)	Moderate COPD (n = 77)	Severe COPD (n = 30)
FVC, %, mean $\pm$ SD	45.5 $\pm$ 12.8	37.2 $\pm$ 6.3*	27.4 $\pm$ 7.9*,†	74.8 $\pm$ 16.5	55.2 $\pm$ 9.1*	45.7 $\pm$ 7.9*,†
FEV ₁ , %, mean $\pm$ SD	43.6 $\pm$ 13.4	38.4 $\pm$ 8.6*	32.7 $\pm$ 8.6*,†	68.7 $\pm$ 16.7	60.8 $\pm$ 16.9*	52.4 $\pm$ 13.5*,†

FVC and FEV₁ are expressed as percentage of preoperative baseline value. POD, Postoperative day; COPD, chronic obstructive pulmonary disease; FVC, forced vital capacity; FEV₁, forced expiratory volume in 1 second; SD, standard deviation. * P < .001 versus no or mild COPD. † P < .05 versus moderate COPD.

TABLE 4. Postoperative outcomes

Outcome	No or mild COPD (n = 144)	Moderate COPD (n = 77)	Severe COPD (n = 30)
Respiratory outcomes, n (%)	13 (9.0)	28 (36.4)	25 (83.3)*,†
Prolonged mechanical ventilation, n (%)	5 (3.5)	6 (7.7)	10 (33.3)*,†
Reintubation, n (%)	1 (0.7)	11 (14.2)*	5 (16.6)*,†
Pneumonia, n (%)	7 (4.8)	11 (14.2)*	10 (33.3)*,†
Hospital LOS, d, mean $\pm$ SD	6.2 $\pm$ 1.6	8.9 $\pm$ 2.4*	12.6 $\pm$ 5.1*,†
Prolonged LOS, n (%)	0 (0)	9 (11.6)*	13 (43.4)*,†

COPD, Chronic obstructive pulmonary disease; LOS, length of stay; SD, standard deviation. * $P < .01$ versus no or mild COPD. † $P < .05$ versus moderate COPD.

by the significant negative correlation between FEV₁ at POD 5 and postoperative LOS.

Previous studies demonstrated an association between COPD and postoperative morbidity and mortality.^{11,12,29} However, the heterogeneity of clinical spirometric variables used to define COPD led to controversial results. Ivanov and colleagues³⁰ evaluated 1412 patients undergoing cardiac surgery and concluded that the Society of Thoracic Surgeon score and pulmonary function tests offer modest discriminatory ability to predict respiratory failure, prolonged postoperative LOS, and 30-day all-cause mortality. However, pulmonary function tests were not performed routinely, and the physicians were not blinded to spirometric results and might have modified treatment strategies.

Manganas and colleagues³¹ retrospectively evaluated patients with COPD after CABG and found that severe COPD was associated with a higher incidence of pneumonia with no difference in mortality and hospital LOS. However, patients with mild and moderate COPD were included in the same group, potentially confounding the results. In our study, both moderate and severe COPD were associated with a higher incidence of pneumonia. Another study³² demonstrated a significantly higher mortality risk with moderate and severe COPD, but spirometry was not routinely performed before cardiac surgery in either study.

Our results indicate that the greater the COPD severity, the greater the impairment in postoperative pulmonary function and, consequently, the worse the outcomes after OPCAB. These findings could be explained by the pathophysiology of the disease. COPD progresses with intrinsic changes in respiratory mechanics and gas exchange, as well as chronic inflammation.¹⁴ This baseline pulmonary dysfunction was likely potentiated by the operation.

The preoperative FEV₁ value must be established as a major prognostic factor for postoperative complications after CABG,¹² given its association with increased LOS and morbidity and mortality.²⁷ Our study corroborates these findings; the adjusted OR for patients with severe COPD (FEV₁ <50%) indicates an elevated risk for developing respiratory outcomes (ie, pneumonia, reintubation, and prolonged mechanical ventilation), increasing LOS. Our MARSplines analysis identified a preoperative FEV₁ cutoff value of approximately 50% of the predicted value as a significant marker for complications following CABG.

In this context, the lack of COPD severity stratification can lead to a misanalysis of preoperative risk, highlighting the clinical importance of preoperative GOLD stratification with FEV₁ evaluation. Recently published guidelines emphasize the importance of spirometry as the gold standard for the diagnosis and staging of severity in patients with COPD; thus, we strongly recommend routine spirometry assessment before cardiac surgery for risk stratification and for specific treatment planning by health professionals.

This study has several limitations. First, the clinicians were not blinded to the spirometry data, which might have influenced postoperative management. Second, almost all of our study patients were male, and the results may differ for female patients. Third, we found that a greater severity of COPD was associated with a lower LVEF, confirming the findings of previous studies.⁶ The fact that LVEF differed across groups might have influenced our results. Nonetheless, severe COPD is associated with lower LVEF and advanced coronary artery disease, likely related to common risk factors linked to their emergence, such as heavy smoking.

TABLE 5. MARSplines analysis to evaluate the prognostic performance of FEV₁ with regard to respiratory outcomes

Variable	OR	95% CI	β value	P value
FEV ₁	0.992	0.987-1.004	-0.008	.001
Age	0.948	0.847-1.061	-0.054	.350
BMI	0.925	0.826-1.035	-0.078	.172
LVEF	0.784	0.697-0.883	-0.244	.003

OR, Odds ratio; CI, confidence interval; FEV₁, forced expiratory volume in 1 second; BMI, body mass index; LVEF, left ventricular ejection fraction.

FIGURE 2. Best found cutoff point that maximizes the optimal sensitivity and specificity for respiratory outcomes. The confounders included in the model were age, body mass index, and left ventricular ejection fraction. FEV_1 , Forced expiratory volume in 1 second.

In conclusion, increased COPD severity was associated with a greater impairment in pulmonary function and worse clinical outcomes in the early postoperative period after OPCAB. A preoperative $FEV_1 < 50\%$ of the predicted value appears to be an important prognostic marker of postoperative complications after surgical myocardial revascularization. Therefore, the preoperative use of spirometry for COPD severity stratification may help refine currently used operative risk scores.

Conflict of Interest Statement

Authors have nothing to disclose with regard to commercial support.

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