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ORIGINAL RESEARCH

Asymptomatic Patients with Airflow Limitation are at Higher Risk of Postoperative Pulmonary Complications After Lung Surgeries: An Ambispective Cohort Study

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Purpose: With the use of pulmonary function tests (PFTs) as a preoperative examination, it is not rare to screen out airflow limitation (AFL) in asymptomatic patients undergoing lung surgeries. This study aims to elucidate whether there is a difference in the prevalence and prognosis of postoperative pulmonary complications (PPCs) between asymptomatic patients with newly diagnosed AFL and the normal population undergoing lung surgeries.

Patients and Methods: The medical records of asymptomatic patients undergoing lung surgeries who were spirometrically diagnosed with AFL between January and October 2017 were collected in Qilu hospital. These patients were subsequently followed up until February 2021. The diagnosis of PPCs was based on a recommended consensus definition. The incidence of PPCs between the newly diagnosed AFL group and the normal group was compared and a propensity score-matched analysis (PSM) was performed. The survival analysis was performed to investigate the long-term prognosis of the two groups.

Results: Overall, 535 asymptomatic subjects were recruited and 126 subjects (11.4%) were spirometrically diagnosed as AFL. The incidence of PPCs was significantly higher in the newly diagnosed AFL group than in the normal population (28.6%VS 14.4%, $P < 0.001$), especially in the $FEV_1/FVC \leq 65\%$ group ($P < 0.001$), which were all confirmed by PSM analysis. Furthermore, these patients were at a higher risk of ICU admissions ($P < 0.001$) and 90-day hospital readmissions secondary to PPCs ($P < 0.001$). No significant differences were found in the overall, in-hospital and 90-day mortality between the AFL group and the normal group (P values >0.05).

Conclusion: Asymptomatic patients with AFL are at higher risk of PPCs than the general population after lung surgeries, along with an increase in ICU admissions and 90-day hospital readmissions secondary to PPCs. Although these patients tended to report worse current conditions, they were similar in the in-hospital, 90-day and overall mortality during the follow-up.

Keywords: pulmonary function tests, newly diagnosed airflow limitation, propensity score-matched analysis, postoperative outcomes

Introduction

As a recommended preoperative examination, pulmonary function tests (PFTs) have been widely performed to predict the incidence of perioperative complications as well as to determine the optimal treatment or surgical method, especially in patients undergoing lung surgeries.[1,2] Along with the routine use of PFTs, it is not rare to screen out airflow limitation (AFL) in asymptomatic patients who have few respiratory symptoms and no diagnosed chronic cardiopulmonary diseases.

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Previous evidence has shown that the incidence of newly diagnosed AFL is far more higher than expected.[3–7] Additionally, GOLD (Global Initiative for Chronic Obstructive Lung Disease) guidelines have indicated that never smokers with chronic airflow limitation may have no increased risk of lung cancer or cardiovascular comorbidities.[1,4,8,9]

Postoperative pulmonary complications (PPCs), whose majority are postoperative pneumonia (POP) and respiratory failure, are common and frequently life-threatening in patients who have undergone lung surgeries,[10–13] with an incidence ranging from 9% to 40% due to the lack of recognized definitions.[14,15] Currently, PPCs have been acknowledged as the leading cause of postoperative morbidity and mortality, associated with additional costs of health care.[13,15,16] Therefore, identifying potent patients at high risk for PPCs is critical to benefiting those patients and thus lowering health costs. As a verified risk factor for the development of PPCs, the presence of chronic obstructive pulmonary diseases (COPD) has a great impact on the prevalence and prognosis of PPCs.[15,17,18] It's noted that patients with COPD may result in an increased risk of pneumonia and mortality from respiratory failure with the progression of the disease.[1,4,9] Preoperative spirometry tests have indicated the presence of AFL in some asymptomatic patients undergoing lung surgeries. However, few attempts have been made to investigate whether these patients are at higher risk of PPCs than the general population after lung surgeries, especially in China. This study aims to elucidate whether there's a difference in the prevalence of PPCs between asymptomatic patients with newly-diagnosed AFL and the normal population undergoing lung surgeries in China. It should be noted that the group of patients without AFL was defined as "normal population". Furthermore, we followed up these patients and evaluated whether the development of AFL had an impact on the long-term life quality and survival after lung surgeries.

Materials and Methods

Study Subjects/Population

This cohort study was conducted between November 2018 and February 2021 in a Chinese tertiary medical center (Qilu Hospital, Shandong University). The medical records of patients who underwent lung surgeries between January and October 2017 were reviewed from a detailed database. Patients who met the following inclusion criteria were included: 1) age between 18 and 80 years old; 2) preoperative PFTs were performed and interpreted strictly under American Thoracic Society (ATS)/European Respiratory Society (ERS) guidelines; 3) the lung surgery was performed under general anesthesia with single lung ventilation. The medical data of 1102 subjects that met the inclusion criteria were systematically reviewed and collected. The exclusion criteria included: 1) self-reported doctor diagnosis of cardiopulmonary diseases, especially the medical history of asthma, chronic bronchitis or emphysema; 2) recent acute respiratory symptoms, particularly cough, phlegm producing or dyspnea in the last 14 days; 3) unsuitable surgical candidates, those who were either physically or mentally intolerant of surgeries; 4) information incomplete or data missing. The study was conducted in accordance with the Declaration of Helsinki. No intervention was performed, and all data in this study were fully anonymized. Written informed consent was obtained from each patient. The study protocol was approved by the Medical Ethics Committee of Qilu Hospital of Shandong University (No. 2018 (143)) and registered at the Chinese clinical trial registry (ChiCTR1800019394) in advance.

Definitions

Newly diagnosed AFL was spirometrically defined as a previously undiagnosed forced expiratory volume in the first second to forced vital capacity ratio (FEV_1/FVC) <70% in the above subjects following the GOLD guidelines.[1,8] All the PFTs were routinely performed under strict quality control following the American Thoracic Society (ATS) guidelines in all the above thoracic surgical candidates. The remaining subjects were allocated to the normal group.

Based on a recommended consensus definition,[14] only respiratory diagnoses that shared common pathophysiological mechanisms were identified as PPCs, which included: 1) atelectasis detected on computed tomography or chest radiograph; 2) pneumonia using US Centers for Disease Control criteria; 3) Acute Respiratory Distress Syndrome using Berlin consensus definition; 4) pulmonary aspiration (a clear clinical history and radiological evidences are essential for the diagnosis).[12] As all the subjects were performed lung surgeries with single lung ventilation, suspected atelectasis without imaging confirmation was not recognized as PPCs.

Data Collection and Follow-Up

The perioperative data of the enrolled subjects were collected, which included: the demographic characteristics, smoking status, comorbidities, American Society of Anesthesiologists (ASA) class, spirometry results, surgical

procedure, surgical method, pathology, analgesia and detailed postoperative outcomes. All the postoperative complications which occurred before discharge, the total length of stay (LOS) in hospital after the date of surgery, intensive care unit (ICU) admission and in-hospital mortality were also recorded in detail.

All patients were annually followed up for overall survival (OS). All the follow-up data were achieved using a telephone questionnaire. The 90-day readmission to hospital secondary to PPCs, current status, ongoing treatment and mortality were enrolled.

Statistical Analysis

For categorical data, data were expressed as counts (proportion) and compared using the chi-square or Fisher's exact tests. The Shapiro–Wilk test was used to test the assumption of normality. For continuous variables, data were expressed as mean ± standard deviation (SD) or medians and compared using Student t or Mann–Whitney *U*-tests in accordance with their distributions, respectively. A stepwise multivariate binary logistic regression analysis was performed to identify the independent predictors of PPCs.

A propensity score-matched analysis (PSM) was performed using a multivariable logistic regression model based on the following cofounders: sex, age, BMI, smoking status, Brinkman Index (BI = cigarette packs smoked per day times years of smoking), diabetes mellitus (DM), hypertension, coronary heart disease (CHD), ischemic cerebrovascular disease (ICVD), ASA class, surgical procedure, surgical method, pathology and analgesia. Pairs of patients with normal spirometry or newly diagnosed AFL were derived using 1:1 greedy nearest neighbor matching within a propensity score of 0.02. This statistical strategy resulted in 121 matched pairs. Comparisons between the matched groups were performed with paired *t*-test or Wilcoxon rank sum test for continuous variables and McNemar test for categorical variables.

The Kaplan–Meier method was used to perform cumulative analyses and differences between groups were assessed with the Log rank test. All the results were considered significant at P value <0.05. All the statistical analyses were performed using IBM SPSS Statistics (version 25.0; IBM, Armonk, NY, USA).

Results

Overall, the medical records of 1102 patients who underwent lung surgeries between January and October 2017 were reviewed. A total of 535 cases were enrolled and 126 subjects (11.4%) were spirometrically diagnosed as AFL (Figure 1). According to the assessment tool recommended by GOLD,[1,8] 74 cases (58.7%) were classified into grade 1, group A (mild),49 cases (38.9%) into grade 2, group C (moderate) and 3 cases (2.4%) into grade 3, group C (severe). As is shown in Table 1, there were significant differences in sex, age and the extent of cigarette exposure (both smoking status and BI)

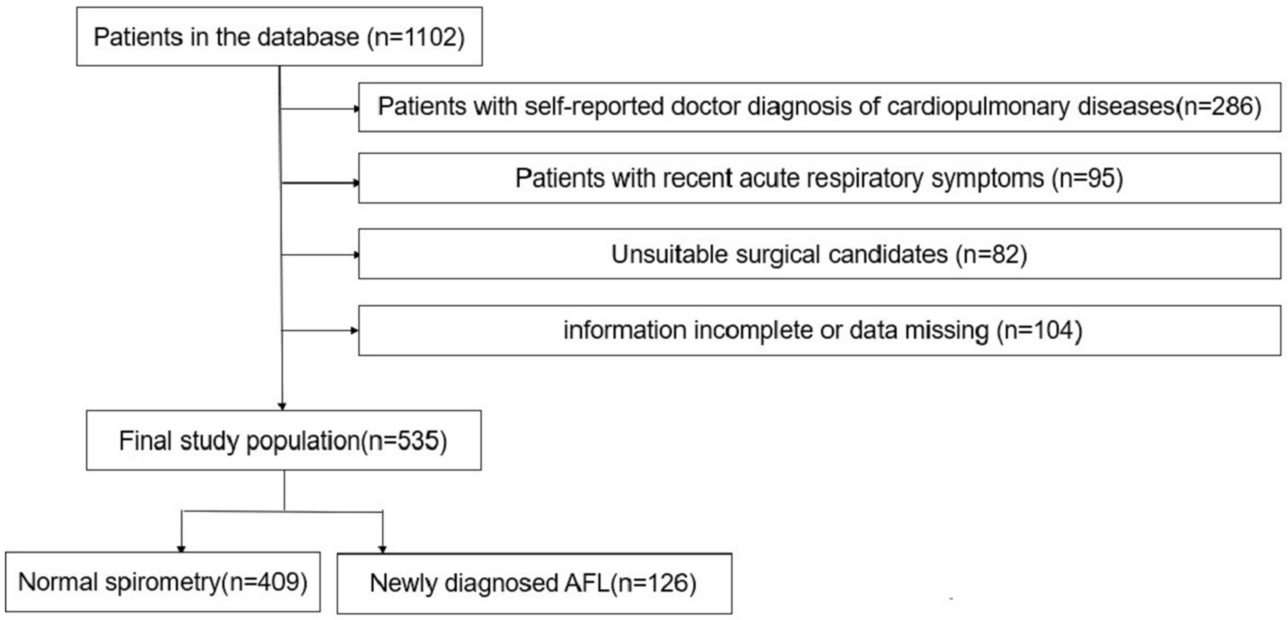

Figure 1 Flowchart of selection of the study population.
Abbreviation: AFL, airflow limitation.

Table 1 Baseline Characteristics of Study Population Prior to Propensity Score-Matching Analysis

	Total (n=535)	Normal Spirometry (n=409)	Newly Diagnosed AFL				P-value
			Total (n=126)	Mild (Group A, n=74)	Moderate to Severe (Group C, n=52)	P-value	
Sex, male	310(57.9)	210(51.3)	100(79.4)	56(75.7)	44(84.6)	0.222	<0.001
Age, years	60(53–65)	59(52–64)	62(55.75–68)	60.45±9.02	62.33±9.93	0.271	<0.001
BMI, kg/m^2	25.08±3.39	25.19±3.34	24.74±3.56	25.23±3.89	24.05±2.91	0.055	0.193
Smoking status							
Never	329(61.5)	282(68.9)	47(37.3)	32(43.2)	15(28.8)	0.202	<0.001
Ex-smoker	16(3.0)	10(2.4)	6(4.8)	4(5.4)	2(3.8)		
Current-smoker	190(35.5)	117(28.6)	73(57.9)	38(51.4)	35(67.3)		
BI	0(0–600)	0(0–375)	400(0–800)	200(0–725)	200(0–700)	0.021	<0.001
≥400	150(28.0)	88(21.5)	64(50.8)	29(39.2)	33(63.5)	0.007	<0.001
<400	385(72.0)	321(78.5)	62(49.2)	45(60.8)	19(36.5)		
Comorbidity							
DM	71(13.3)	52(12.7)	19(15.1)	10(13.5)	9(17.3)	0.558	0.494
Hypertension	124(23.2)	86(21.0)	38(30.2)	19(25.7)	19(36.5)	0.191	0.034
CHD	55(10.3)	41(10.0)	14(11.1)	8(10.8)	6(11.5)	0.898	0.725
ICVD	22(4.1)	18(4.4)	4(3.2)	3(4.1)	1(1.9)	0.502	0.544
ASA class							
I, II	522(97.4)	400(97.8)	122(96.8)	73(98.6)	49(94.2)	0.305	0.516
III	13(2.4)	9(2.2)	4(3.2)	1(1.4)	3(5.8)		
Perioperative pulmonary function							
FEV_1/FVC	75.77±8.09	79.19±5.11	64.67±5.66	67.11±2.62	61.20±6.92	<0.001	<0.001
FEV_1%pred	100.08±19.05	104.99±16.84	84.13±16.99	94.60±12.80	69.22±9.36	<0.001	<0.001
Surgical procedure							
Lobectomy	454(84.9)	346(84.6)	108(85.7)	68(91.9)	40(76.9)	0.023	0.406
Subsegmentectomy/ wedge	55(10.3)	44(10.8)	11(8.7)	2(2.7)	9(17.3)		
Pneumonectomy	17(3.2)	14(3.4)	3(2.4)	1(1.4)	2(3.8)		
Others	9(1.7)	5(1.2)	4(3.2)	3(4.1)	1(1.9)		
Surgical method							
VATS	445(83.2)	349(85.3)	96(76.2)	56(75.7)	40(76.9)	0.871	0.016
Open surgery	90(16.8)	60(14.7)	30(23.8)	18(24.3)	12(23.1)		
Pathology							
NSCLC							
Adenocarcinoma	356(66.5)	273(66.7)	83(65.9)	49(66.2)	34(64.5)	0.529	0.317
Squamous	106(19.8)	75(18.3)	31(24.6)	20(27.0)	11(21.2)		
Other NSCLC	9(1.7)	6(1.5)	3(2.4)	2(2.7)	1(1.9)		
Metastatic disease	10(1.9)	8(2.0)	2(1.6)	1(1.4)	1(1.9)		
Benign tumor	41(7.7)	36(8.8)	5(4.0)	2(2.7)	3(5.8)		
Others	13(2.4)	11(2.7)	2(1.6)	0(0.0)	2(3.8)		
Analgesia							
PCA only	346(64.7)	265(64.8)	81(64.3)	44(59.5)	37(71.2)	0.382	0.930
Epidural +PCA	165(30.8)	125(30.6)	40(31.7)	27(36.5)	13(25.0)		
Nerve block +PCA	24(4.5)	19(4.6)	5(4.0)	3(4.1)	2(3.8)		

Notes: Data are expressed as mean ± SD or medians with an interquartile range (25–75).

Abbreviations: BMI, body mass index; BI, Brinkman Index; ICVD, ischemic cerebrovascular disease; DM, diabetes mellitus; CHD, coronary heart disease; ASA, American Society of Anesthesiologists; VATS, video-assisted thoracoscopic surgery; NSCLC, non-small cell lung cancer; PCA, patient-controlled analgesia.

between subjects with AFL and normal spirometry. However, no significant differences were found between group A and group C, except for BI($P < 0.05$). Tables 1 and 2 show the baseline characteristics before and after PSM analysis, respectively. After PSM analysis, both groups were well matched in all the baseline parameters concerned (P values >0.05).

Table 2 Baseline Characteristics of Study Patients After Propensity Score-Match Analysis

Total (n=242)	Normal Spirometry (n=121)	Newly Diagnosed AFL (n=121)	P-value
Sex, male	97(80.2)	95(78.5)	0.815
Age, years	62.07±8.10	60.93±9.42	0.276
BMI, kg/m^2	24.78±3.03	24.74±3.48	0.923
Smoking status			
Never	55(45.5)	46(38.0)	0.425
Ex-smoker	6(5.0)	6(5.0)	
Current-smoker	60(49.6)	69(57.0)	
Brinkman Index	200(0–800)	400(0–800)	0.915
≥400	50(41.3)	58(47.9)	0.229
<400	71(58.7)	63(52.1)	
Comorbidity			
DM	23(19.0)	19(15.7)	0.627
Hypertension	30(24.8)	36(29.8)	0.451
CHD	21(17.4)	14(11.6)	0.281
ICVD	4(3.3)	4(3.3)	1.000
ASA class			
I, II	119(98.3)	117(96.7)	0.687
III	2(1.7)	4(3.3)	
Perioperative pulmonary function			
FEV_1/FVC	74.24±3.08	64.57±5.73	<0.001
FEV_1%pred	99.62±26.50	83.73±17.17	<0.001
Surgical procedure			
Lobectomy	104(86.0)	103(85.1)	0.549
Subsegmentectomy/wedge	10(8.3)	11(9.1)	
Pneumonectomy	5(4.1)	3(2.5)	
Others	2(1.7)	4(3.3)	
Surgical method			
VATS	96(79.3)	93(76.9)	0.749
Open surgery	25(20.7)	28(23.1)	
Pathology			
NSCLC			
Adenocarcinoma	76(62.8)	80(66.1)	0.780
Squamous	31(25.6)	29(24.0)	
Other NSCLC	3(2.5)	3(2.5)	
Metastatic disease	1(0.8)	2(1.7)	
Benign tumor	9(7.4)	5(4.1)	
Others	1(0.8)	2(1.7)	
Analgesia			
PCA only	79(65.3)	78(64.5)	0.412
Epidural +PCA	41(33.9)	38(31.4)	
Nerve block +PCA	1(0.8)	5(4.1)	

Notes: Data are expressed as mean ± SD or medians with an interquartile range (25–75).

Abbreviations: BMI, body mass index; BI, Brinkman Index; ICVD, ischemic cerebrovascular disease; DM, diabetes mellitus; CHD, coronary heart disease; ASA, American Society of Anesthesiologists; VATS, video-assisted thoracoscopic surgery; NSCLC, non-small cell lung cancer; PCA, patient-controlled analgesia.

The stepwise multivariate logistic regression indicated that age and AFL were independent predictors of PPCs (Table 3). Compared with the normal population, patients with newly diagnosed AFL were 1.79 times more likely to develop PPCs (95% CI 1.07 to 3.00, P = 0.026). Meanwhile, elderly patients were 1.04 times more likely to develop PPCs in comparison with the normal group (95% CI 1.01 to 1.07, P = 0.003).

Based on the above-mentioned consensus definition, a total of 95 subjects (17.7%) had the clinical evidence of PPCs, with a significant increase in the newly diagnosed AFL group (28.6%VS 14.4%, P < 0.001). As is shown in Table 4, the majority of PPCs were POP (n = 82, 15.3%), followed by respiratory failure (n = 7, 1.3%), atelectasis (n = 5, 0.9%) and aspiration (n = 1, 0.2%). Patients in the newly diagnosed AFL group had a longer LOS after surgery (10 (9 to 11) vs 11 (9 to 13.25), P < 0.001), significantly higher rates of ICU admissions (15.1% vs 4.9%, P < 0.001), tracheal intubation (1.6% vs 1.0%, P = 0.001) and 90-day hospital readmissions secondary to PPCs (7.9% vs 0.7%, P < 0.001). Furthermore, among the AFL group, the prevalence of PPCs remained significantly higher among those in the $FEV_1/FVC \leq 65\%$ group with the decline in FEV_1/FVC (P < 0.001), which was in accordance with the higher rates of ICU admissions (P = 0.002), tracheal intubation (P = 0.002) and 90-day hospital readmissions secondary to PPCs (P = 0.005).

Patients with AFL tended to suffer from a worse self-reported current status than the normal population (P = 0.028, Table 4). A total of 74 patients (13.8%) died during follow-up, 18 cases were from the newly diagnosed AFL group, while the remaining 56 cases were from the normal group (14.3% vs 13.7%, P = 0.866). Causes of death included PPC-related deaths (4, 0.7%), surgery-related deaths (2, 0.4%), cancer-related deaths (59,11.0%) and others (9, 1.7%). There were no significant differences in the overall mortality, in-hospital mortality, 90-day mortality and causes of death between the AFL group and the normal group (P values >0.05, Table 4). Furthermore, no significant differences were found with the decline of FEV_1/FVC ratios concerning the above mortalities (P values >0.05, Table 4). All the patients were followed up for 41 to 49 months, the overall survival (cumulative survival rates) was not significantly different between the AFL group and the normal group before and after PSM analysis (P = 0.781, Figure 2 and P = 0.092, Figure 3).

After PSM analysis, the prevalence of PPCs in the AFL group was still significantly higher than that in the normal group (P < 0.001), along with an increase in ICU admissions (P = 0.049) and 90-day hospital readmissions secondary to PPCs (P = 0.021, Table 5). However, there was no significant difference in the mean LOS between the two groups after PSM analysis (P = 0.067, Table 5).

Discussion

A total of up to 11.4% (126/535) patients undergoing lung surgeries were spirometrically diagnosed as AFL using the fixed ratio (FEV_1/FVC <70%) though preoperative spirometry and the incidence were in accordance with previous studies.[3,4,6,19] Generally, elderly males with higher levels of tobacco exposure tended to suffer from AFL. Our study confirmed that asymptomatic patients with AFL were at higher risk of PPCs than the general population in those who had undergone lung surgeries, accompanied by an

Table 3 Multivariate Logistic Regression Analysis to Assess Predictors of PPCs

Variable	β	Wald	P-value	OR	95% CI
Age	0.040	8.627	0.003	1.041	1.013–1.069
Male	0.057	0.040	0.841	1.059	0.604–1.856
ASA III	−0.843	1.705	0.192	0.430	0.121–1.526
Newly diagnosed AFL	0.585	4.955	0.026	1.794	1.072–3.002
BI≥400	0.414	2.191	0.139	1.513	0.874–2.617
Lobectomy			0.803		
Subsegmentectomy/wedge	0.220	0.361	0.548	1.246	0.607–2.557
Pneumectomy	0.492	0.710	0.400	1.635	0.521–5.131
Other surgical procedures	0.056	0.004	0.947	1.508	0.203–5.500

Abbreviations: ASA, American Society of Anesthesiologists; AFL, airflow limitation; BI, Brinkman Index; OR, odds ratio; CI, confidence index.

Table 4 Postoperative Outcomes Prior to Propensity Score-Match Analysis

	Total (n=535)	Normal Spirometry (n=409)	Newly Diagnosed AFL				P-value
			Total (n=126)	65%<FEV_1/FVC < 70% (n=80)	FEV_1/FVC ≤65% (n=46)	P-value	
Mean LOS (days)	10(9–12)	10(9–11)	11(9–13.25)	10(9–13)	11(8–15)	0.177	<0.001
Overall in-hospital complications							
PPCs (at least one)	95(17.8)	59(14.4)	36(28.6)	15(18.8)	21(45.7)	<0.001	<0.001
POP	82(15.3)	51(12.5)	31(24.6)	14(17.5)	17(37.0)	<0.001	<0.001
Respiratory failure	7(1.3)	3(0.7)	4(3.2)	0(0)	4(8.7)		
Atelectasis	5(0.9)	4(1.0)	1(0.8)	1(1.3)	0(0)		
Pulmonary aspiration	1(0.2)	1(0.2)	0(0)	0(0)	0(0)		
Atrial fibrillation	3(0.6)	2(0.5)	1(0.8)	1(1.3)	0(0)	0.446	0.689
Acute myocardial infarction	2(0.4)	1(0.2)	1(0.8)	0(0)	1(2.2)	0.186	0.377
Aortic dissection	1(0.2)	1(0.2)	0(0)	0(0)	0(0)	1.000	0.578
Bronchopleural fistula	1(0.2)	0(0)	1(0.8)	0(0)	1(2.2)	0.186	0.072
Pulmonary embolism	1(0.2)	1(0.2)	0(0)	0(0)	0(0)	1.000	0.578
ICU admissions	39(7.3)	20(4.9)	19(15.1)	6(7.5)	13(28.3)	0.002	<0.001
Tracheal intubation	6(1.1)	4(1.0)	2(1.6)	0(0)	2(4.3)	0.002	0.001
90-day hospital readmissions secondary to PPCs	14(2.6)	4(0.7)	10(7.9)	2(2.5)	8(17.4)	0.005	<0.001
Current status (quality of life)							
In good condition	370(69.2)	283(69.2)	87(69.0)	58(72.5)	29(63.0)	0.435	0.028
Out of condition	31(5.8)	18(4.4)	13(10.3)	7(8.8)	6(13.0)		
Mortality							
Total	74(13.8)	56(13.7)	18(14.3)	9(11.3)	9(19.6)	0.164	0.866
In-hospital mortality	4(0.7)	3(0.7)	1(0.8)	0(0)	1(2.2)		0.944
90-day mortality	9(1.7)	7(1.7)	2(1.6)	0(0)	2(4.3)		0.924
Causes of death							
PPCs	4(0.7)	3(0.7)	1(0.8)	0(0)	1(2.2)	0.186	0.944
Surgery-related	2(0.4)	1(0.2)	1(0.8)	0(0)	1(2.2)		0.377
Cancer-related	59(11.0)	46(11.2)	13(10.3)	7(8.8)	6(13.0)		0.771
Others							
Respiratory	3(0.6)	2(0.5)	1(0.8)	0(0)	1(2.2)		0.689
Cardiovascular	2(0.4)	1(0.2)	1(0.8)	1(1.3)	0(0)		0.377
Others	4(0.7)	3(0.7)	1(0.8)	1(1.3)	0(0)		0.944

Notes: Data are expressed as medians with an interquartile range (25–75).
Abbreviations: PPC, postoperative pulmonary complications; AFL, airflow limitation; LOS, the total length of stay in hospital after the date of surgery; POP, postoperative pneumonia.

increase in ICU admissions and 90-day hospital readmissions secondary to PPCs both before and after PSM analysis.

GOLD guidelines recommended the use of post-bronchodilator spirometry test and the fixed ratio as cutoff point (instead of lower limit of normal (LLN)) to confirm the presence of persistent airflow limitation.[1,2,8] However, only pre-bronchodilator values were achieved in our study, similar to most published studies. Previous studies had shown that reversible obstruction accounted for approximately 35% and the corresponding post-bronchodilator FEV_1/FVC ratios would return to the normal range (beyond 70%).[20,21] On the other hand, it was reported that up to 93% individuals could be diagnosed as irreversible AFL if the cutoff value of prebronchodilator FEV_1/FVC ratios were set as 65%.[20,22] To avoid potential overestimation of AFL, we divided the newly diagnosed AFL group into two groups based on the decline of FEV_1/FVC ratios (1. those lower than 65%; 2. those between 65% and 70%) and made a comparison.

One highlight of the present study was the definition of PPCs we applied. Numerous postoperative pulmonary outcome measures were used in previous studies, but many were imprecise and poorly defined. The lack of recognized

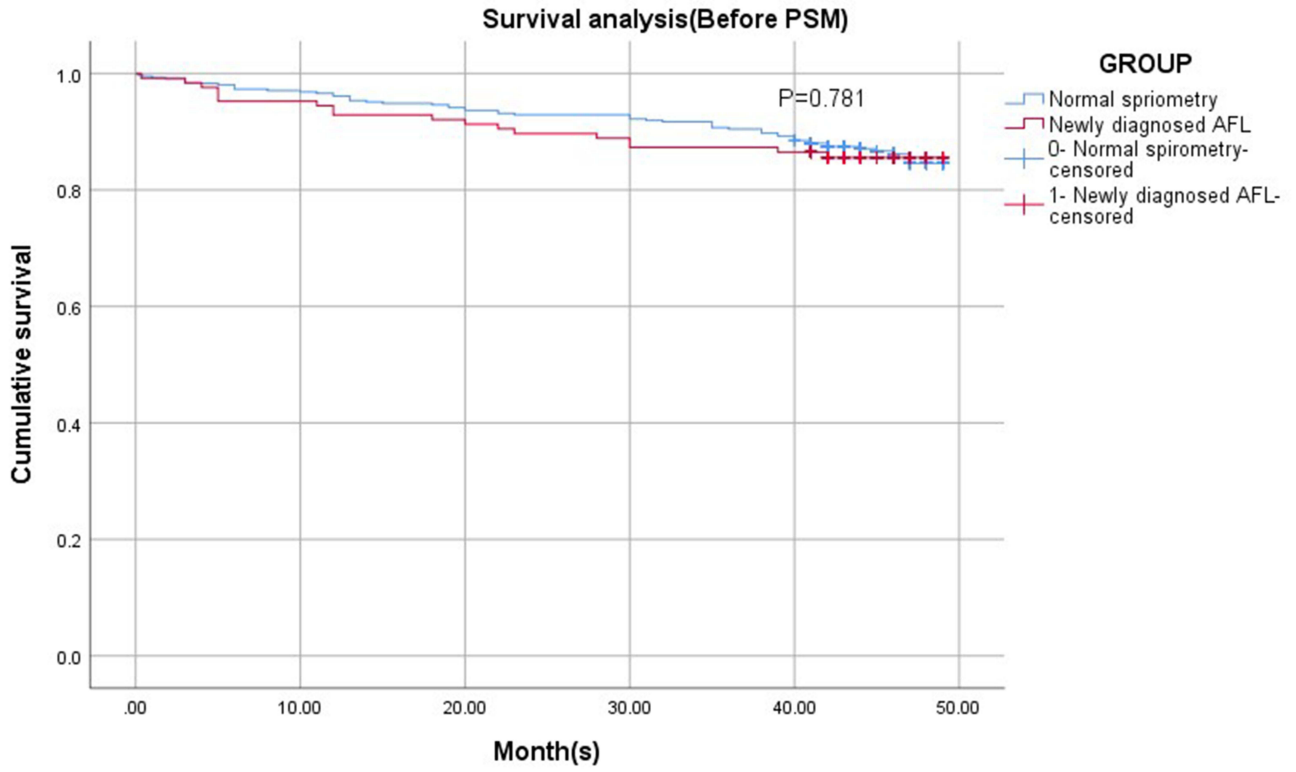

Figure 2 Kaplan-Meier cumulative event curves of all-cause death before propensity score-matching.
Abbreviations: PSM, propensity score-matched analysis; AFL, airflow limitation.

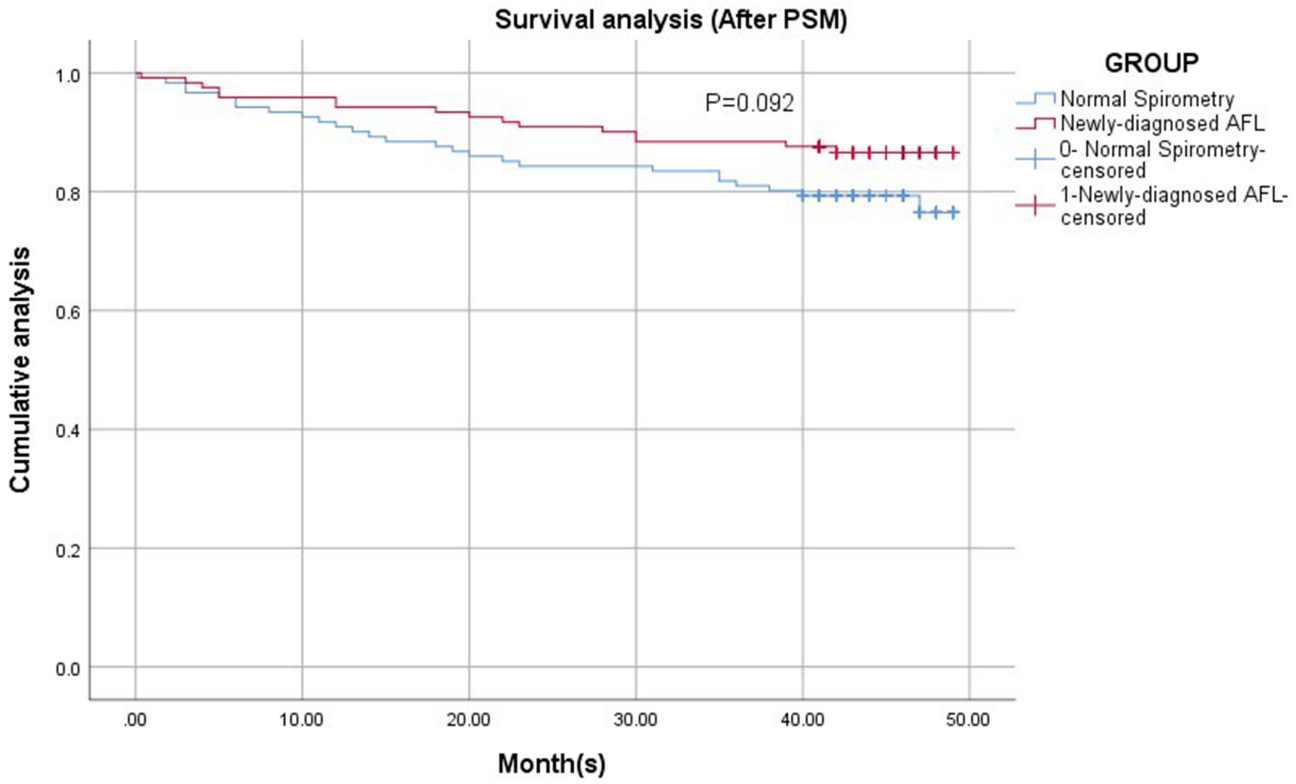

Figure 3 Kaplan-Meier cumulative event curves of all-cause death after propensity score-matching.
Abbreviations: PSM, propensity score-matched analysis; AFL, airflow limitation.

Table 5 Postoperative Outcomes After Propensity Score-Match Analysis

	Normal Spirometry (n=121)	Newly Diagnosed AFL (n=121)	P-value
Mean LOS (days)	10(9–12)	11(9–13)	0.067
Overall in-hospital complications			
PPCs	21(17.3)	35(28.9)	<0.001
ICU admissions	9(7.4)	18(14.8)	0.049
90-day hospital readmissions secondary to PPCs	2(1.7)	10(8.3)	0.021

Notes: Data are expressed as medians with an interquartile range (25–75).
Abbreviations: AFL, airflow limitation; LOS, the total length of stay in hospital after the date of surgery; PPC, postoperative pulmonary complications.

consensus definitions resulted in great differences in the prevalence of PPCs, which varied from 9% to 40%.[14,15] After performing a systematic literature review and a three-stage Delphi consensus process, Abbott and his colleagues selected a set of recognized and precise definitions for perioperative complications.[14] Our study took the lead to apply this set of recommended definitions to Chinese patients in order to improve our design and avoid misdiagnosis of PPCs.

Our study confirmed that the prevalence of PPCs, ICU admissions, tracheal intubation and 90-day hospital readmissions secondary to PPCs remained significantly higher in patients with newly diagnosed airflow limitation than the normal group, with the decline of FEV_1/FVC ratio. Patients in the newly diagnosed group tended to have a longer LOS, but no significant difference was found after PSM analysis. Some patients in the matched pairs received postoperative chemotherapy and resulted in a prolonged LOS in the normal group, which could partly explain the above-mentioned discrepancy.

It is noteworthy that two patients with moderate-to-severe airflow limitation discharged without occurrence of PPCs, ICU admissions, prolonged LOS or 90-day readmissions after standardized preoperative inhalation treatment. Although both patients reported few preoperative respiratory symptoms, they were spirometrically diagnosed with moderate-to-severe airflow limitation. Although their lung function showed no obvious improvement after inhalation treatment, both short-term and long-term prognosis were desirable. This implied that standardized preoperative inhalation treatment might be taken into consideration as an effective way to reduce the incidence of PPCs and benefit potential patients. In future, more relevant RCTs (randomized controlled trial) are in urgent need to verify our assumptions.

Our study confirmed that newly diagnosed AFL was an independent predictor of PPCs in asymptomatic patients undergoing lung surgeries. Consistent with previous studies, age was also found to be associated with the development of PPCs, which indicated even elderly healthy patients were at higher risk of PPCs.[12,15,23] However, when age was regarded as the predictor of PPCs, OR was only 1.04 (95% CI 1.01 to 1.07, P = 0.003). One possible explanation is the absence of age stratification. In the meantime, larger sample size would be another solution. It is generally accepted that better functional preservation is accompanied by less reduction in the volume of surgery. Patients scheduled for pneumonectomy are considered as the most likely to suffer from PPCs, 30-day mortality and worse long-term prognosis.[24–26] It's also demonstrated that segmentectomy is recommended for patients with a normal predicted postoperative FEV_1 (% $ppoFEV_1$) while offers no functional advantages over lobectomy in patients with the %$ppoFEV_1$ under 70%.[27] However, our study indicated that surgical procedures were not significantly associated with the incidence of PPCs, tracheal intubation or repeated hospitalization. The majority of patients (454/535, 84.9%) were indicated for lobectomy, while only very few patients underwent pneumonectomy (17/535, 3.2%). This bias might be a possible reason.

To our knowledge, few attempts have been made to investigate the long-term impact of airflow limitation after lung surgeries in China. Recent studies have shown that PPCs are predictors of both short-term and long-term postoperative outcomes and are associated with increased risk of ICU admissions and prolonged LOS.[16,23] Sebastian and his colleagues indicated that the development of PPCs after thoracic surgery was associated with a worse long-term survival and these patients were more likely to die of non-cancer-related deaths.[12] However, previous studies did not elucidate whether the development of AFL had an impact on the long-term quality of life and our study explored this issue. Although patients with AFL tended

to report worse current condition than the normal population during the follow-up, they were similar in in-hospital, 90-day, overall mortality and cumulative survival rates. A large proportion of patients who underwent lung surgeries in our study were generally in good condition and admitted to hospital due to early detection of lung tumor after routine physical examinations. Most of them received clinical recovery after surgical removal and benefited from early diagnosis. This might account for our findings on the similarity in long-term survival between the AFL group and the normal population. In our view, PPC-related deaths (included in the non-cancer-related deaths) were more likely to occur during hospital stay and 90 days after surgery. However, it remains to be elucidated whether the sample size and multicenter trials would make a difference.

It is well documented that the incidence of newly diagnosed AFL is far more higher than expected. Relatively little is understood about these asymptomatic patients, and they definitely deserve more attention. Our study confirmed that the detection of AFL in asymptomatic patients undergoing lung surgeries was an effective way to identify potential patients at high risk for PPCs. According to our findings, we hypothesize that these asymptomatic surgical candidates would benefit from early diagnosis of AFL and early treatment (standardized preoperative inhalation treatment). If so, in order to reduce the incidence of PPCs, spirometry could be performed as a screening tool for patients at high risk and preoperative inhalation treatment could be recommended for asymptomatic patients with newly diagnosed AFL. It implied that this might be an effective way to benefit potential patients and lower medical costs in the long run. There is an urgent need for more well-designed clinical trials to test our hypothesis.

Our study had several limitations. As an ambispective study, some data were retrospectively achieved and the best choice would be RCT. PSM analysis was performed to minimize confounding bias in patient selection, but unknown confounders might exist. At present, PSM analysis could be an acceptable alternative and relative prospective RCTs are in high demand in future. Secondly, as a single-center study, we lacked the external validity required to support widespread changes in practice. Large-scale, multicenter trials are in urgent need to verify our findings and assumptions about inhalation treatment. Thirdly, extended follow-up could be necessary to demonstrate the long-term impact of AFL on survival after lung surgeries.

Conclusion

Our study confirmed that asymptomatic patients with AFL are at higher risk of PPCs than the general population in those who had undergone lung surgeries, accompanied by an increase in ICU admissions and 90-day hospital readmissions secondary to PPCs. Although patients with AFL tended to report worse current condition than the normal population, they were similar in the in-hospital, 90-day and overall mortality during the follow-up.

Data Sharing Statement

We would like to share the individual participant data that underlie the results reported in this article, after deidentification. The study protocol will also be available. The data will be available following article publication. Proposals could be directed to Dr Jinhui Yu yujingui1109@126.com. To gain access, data requestors will need to sign a data access agreement and reasonable requests will be met.

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Disclosure

The authors declare no conflicts of interest in this work.

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