BMJ Open

Mortality and readmission risk for hospitalised patients with acute exacerbation of COPD with and without spirometric obstruction: a longitudinal observational study in China

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To cite: Ren X, Wang Y, He R, *et al*. Mortality and readmission risk for hospitalised patients with acute exacerbation of COPD with and without spirometric obstruction: a longitudinal observational study in China. *BMJ Open* 2023;**13**:e071560. doi:10.1136/bmjopen-2023-071560

► Prepublication history for this paper is available online. To view these files, please visit the journal online (http://dx.doi.org/10.1136/bmjopen-2023-071560).

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Received 06 January 2023
Accepted 09 May 2023

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ABSTRACT

Objective To compare the clinical features and outcomes in patients with pre-chronic obstructive pulmonary disease (COPD) and COPD hospitalised for confirmed or suspected acute exacerbation of COPD (AECOPD).

Design A multicentre, longitudinal observational cohort study.

Setting Data were obtained from the AECOPD Inpatient Registry Study in China.

Participants 5896 patients hospitalised for AECOPD between 2017 and 2021.

Outcomes Patients were divided into the COPD (n=5201) and pre-COPD (n=695) groups according to the lung function test results. The outcomes of interest included all-cause, respiratory disease-related and cardiovascular disease-related deaths as well as readmissions within 30 days and 12 months after discharge. Cumulative incidence functions were used to estimate the risk of cause-specific mortality and readmission. Multivariate hazard function models were used to determine the association between lung function and outcomes.

Results There were significant between-group differences in the symptoms at admission and medication use during hospitalisation. However, there was no significant between-group difference in the 30-day all-cause mortality (0.00 vs 2.23/1000 person-month (pm), p=0.6110) and readmission (33.52 vs 30.64/1000 pm, p=0.7175). Likewise, the 30-day and 12-month cause-specific outcomes were not significantly different between groups (30-day readmission with acute exacerbation (AE): 26.07 vs 25.11/1000 pm; 12-month all-cause mortality: 0.20 vs 0.93/1000 pm; all-cause readmission: 11.49 vs 13.75/1000 pm; readmission with AE: 9.15 vs 11.64/1000 pm, p>0.05 for all comparisons). Cumulative incidence curves revealed no significant between-group differences in the 30-day and 12-month prognosis (p>0.05). Multivariate analysis revealed no significant association of lung function categories with 30-day and 12-month mortality or readmission (p>0.05 for all effect estimations).

Conclusions Patients with pre-COPD have mild symptoms and similar risks for mortality and readmission during follow-up as patients with COPD. Patients with pre-COPD should receive optimal therapies before the occurrence of irreversible damage.

STRENGTHS AND LIMITATIONS OF THIS STUDY

⇒ The study comprehensively compared patients with pre-chronic obstructive pulmonary disease (COPD) and patients with COPD using large-scale real-world registry data in China.
⇒ This study is limited by the follow-up duration required to observe COPD development in patients with pre-COPD.
⇒ We could not evaluate the longitudinal trajectories of patients with pre-COPD given the lack of repeated measurements.

INTRODUCTION

Chronic obstructive pulmonary disease (COPD) is a heterogeneous condition that is mainly caused by exposure to toxic gases and particles and is characterised by chronic respiratory symptoms and progressive airflow obstruction.[1] The latest Chinese epidemiological survey reported that the COPD prevalence increased from 8.2% in 2007 to 13.7% among people aged >40 years.[2] COPD is expected to be the third leading mortality cause worldwide by 2030.[3 4] Accordingly, COPD exerts substantial economic and societal burdens.

A critical issue in the management of patients with COPD is that they are often diagnosed late after severe progression of their symptoms and/or acute exacerbations (AEs), which limits the benefits obtained from existing treatments.[5] Therefore, it is important to promptly identify individuals at significant risk of developing airflow obstruction. Accordingly, the term 'pre-COPD' has been proposed to define the stage when an

individual is at increased risk of COPD,[6] which is characterised by respiratory symptoms with/without detectable structural and/or functional abnormalities but without obstruction (forced expiratory volume in one second (FEV_1)/forced vital capacity (FVC) >0.7).[7]

Patients with pre-COPD are characterised by specific respiratory symptoms, lung function impairment and imaging abnormalities.[8–11] Regarding respiratory symptoms, patients with pre-COPD present cough, sputum production and chronic productive cough for several years prior to meeting the spirometric criteria for COPD diagnosis.[12 13] Moreover, some patients with pre-COPD may not present obvious airflow limitation but show low-to-normal FEV_1, diffusing capacity of the lungs for carbon monoxide and/or accelerated FEV_1 decline.[7] Furthermore, patients with pre-COPD may present radiographic abnormalities such as airway wall thickening, small airway abnormality and emphysema.[14–16] Nonetheless, the defining characteristics of patients with pre-COPD remain to be established.

To address the knowledge gaps about clinical outcomes associated with pre-COPD in the Chinese population, we analysed data from the AEs of COPD Inpatient Registry (ACURE) study, in which a large sample of adults from 179 hospitals dispersed over 28 provinces were collected and represented the major Chinese AE of COPD (AECOPD) population.[17] To determine the basic characteristics of pre-COPD patients, the present study aimed to detect the clinical outcomes of pre-COPD, including respiratory-related and cardiovascular-related readmission and mortality, compared with the COPD population.

METHODS

Study design and participants

A real-world dataset was obtained from the ACURE study, which is an ongoing nationwide multicentre prospective observational cohort study. The ACURE study was designed to explore the prognosis of hospitalised patients with AECOPD in real-world settings in China (ClinicalTrials.gov identifier: NCT02657525). Details regarding the study protocol have been described elsewhere.[17] The ACURE study began enrolling participants on 1 September 2017 and expects to recruit 7600 patients with a 3-year follow-up period.

We analysed longitudinal data obtained until November 2021 from 179 secondary and tertiary hospitals distributed across 28 provinces in China.

The inclusion criteria were as follows: (1) age ≥18 years, (2) hospitalisation for confirmed or suspected AECOPD and (3) having provided consent for participation. We excluded patients who had participated in other clinical trials or interventional studies as well as those diagnosed with clinical conditions that may mimic AECOPD symptoms, including heart failure, pneumonia, asthma or pulmonary embolism. Additionally, we excluded patients who did not undergo pulmonary function tests during hospitalisation or within 30 days of discharge. Among 8372 patients screened in the ACURE dataset, we included 5896 patients eligible for enrolment (figure 1).

Based on clinical symptoms and pulmonary function test results, participants were assigned to the pre-COPD group if they were (1) hospitalised for AE of suspected/confirmed COPD and (2) prebronchodilator or

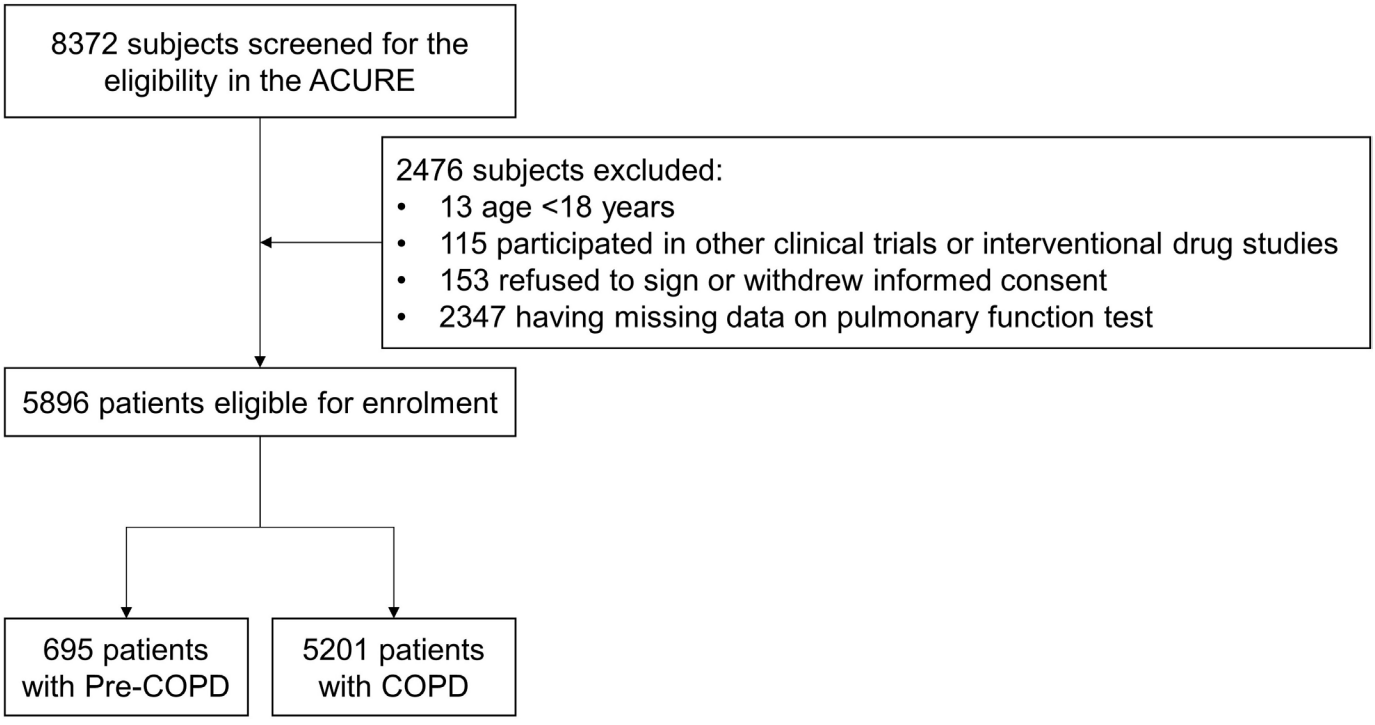

Figure 1 Study participant flowchart. ACURE, Acute Exacerbations of Chronic Obstructive Pulmonary Disease Inpatient Registry; COPD, chronic obstructive pulmonary disease.

Table 1 Baseline characteristics of the overall patient population and each group

Characteristics	Overall (n=5896)	Pre-COPD (n=695)	COPD (n=5201)	p value
Age, years, mean±SD	68.51±9.62	68.98±10.67	68.44±9.47	0.1687
Age group (years), number (%)				0.0002
<50	179 (3.04)	32 (4.60)	147 (2.83)	
50–59	812 (13.77)	90 (12.95)	722 (13.88)	
60–69	2186 (37.08)	218 (31.37)	1968 (37.84)	
70–79	1945 (32.99)	238 (34.24)	1707 (32.82)	
≥ 80	774 (13.13)	117 (16.83)	657 (12.63)	
Men, number (%)	4521 (76.68)	446 (64.17)	4075 (78.35)	<0.0001
Education, number (%)				0.8434
Primary school and below	2803 (47.54)	329 (47.34)	2474 (47.57)	
Junior high school	1851 (31.39)	214 (30.79)	1637 (31.47)	
Senior high school and above	1242 (21.07)	152 (21.87)	1090 (20.96)	
BMI, kg/m^2, mean±SD	22.41±3.88	22.88±4.33	22.35±3.81	0.0007
Smoking status, number (%)				<0.0001
Current smoker	1508 (25.58)	123 (17.70)	1385 (26.63)	
Ex-smoker	2352 (39.89)	219 (31.51)	2133 (41.01)	
Never smoking	2036 (34.53)	353 (50.79)	1683 (32.36)	
FEV_1% predicted, median (quartile)	44.75 (32.33, 62.50)	68.42 (46.80, 90.58)	42.86 (31.56, 58.82)	<0.0001
Pre-existing comorbidities, number (%)				
Asthma	575 (9.75)	51 (7.34)	524 (10.07)	0.0224
Hypertension	1939 (32.89)	242 (34.82)	1697 (32.63)	0.2480
Cardiovascular diseases	2826 (47.93)	348 (50.07)	2478 (47.64)	0.2290
Coronary heart disease	993 (16.84)	152 (21.87)	841 (16.17)	0.0002
Pulmonary artery hypertension	770 (13.06)	87 (12.52)	683 (13.13)	0.6518
Heart failure	22 (0.37)	2 (0.29)	20 (0.38)	0.6943
Atrial fibrillation	172 (2.92)	25 (3.60)	147 (2.83)	0.2568
Right bundle branch block	121 (2.05)	13 (1.87)	108 (2.08)	0.7190
Premature ventricular contraction	95 (1.61)	10 (1.44)	85 (1.63)	0.7007
Digestive diseases	211 (3.58)	21 (3.02)	190 (3.65)	0.3999
Gastro-oesophageal reflux disease	110 (1.87)	10 (1.44)	100 (1.92)	0.3759
Osteoporosis	51 (0.86)	8 (1.15)	43 (0.83)	0.3858
Diabetes	599 (10.16)	81 (11.65)	518 (9.96)	0.1648

BMI, body mass index; COPD, chronic obstructive pulmonary disease; FEV_1, forced expiratory volume in one second.

postbronchodilator $FEV_1/FVC \geq 0.7$. Conversely, patients with postbronchodilator $FEV_1/FVC < 0.7$ were assigned to the COPD group. Group allocation did not consider the bronchodilator test results.

Outcomes and follow-up

According to the protocol, the patients were required to complete face-to-face visits at 30 days (±2 days in practice) and 12 months (±24 days in practice) after discharge. The study outcomes were the 30-day and 12-month mortality and readmission rates. Moreover, the cause-specific mortality, readmission and date of recurrence after discharge were recorded. We primarily focused on all-cause, respiratory-related (COPD, pneumonia, respiratory failure, asthma and lung cancer) and cardiovascular-related (acute myocardial infarction, malignant arrhythmia and heart failure) mortality and readmission. The occurrence of all-cause death was a competing risk for other outcomes in the analysis.

Covariates

All participants underwent in-depth interviews at admission, where their demographic characteristics, symptom severity, medical history and health check-up information were collected. Additionally, the full course of patient treatment during hospitalisation and outcomes at discharge were recorded. The covariates of interest included age (per 10 years, coded as a categorical

Table 2 Clinical characteristics associated with lung function category

Characteristics	Overall (n=5896)	Pre-COPD (n=695)	COPD (n=5201)	p value
Symptoms at admission, number (%)				
Increased cough	3557 (60.33)	400 (57.55)	3157 (60.70)	0.1113
Increased sputum volume	2330 (39.52)	246 (35.40)	2084 (40.07)	0.0179
Increased sputum purulence	2497 (42.35)	247 (35.54)	2250 (43.26)	0.0001
Wheezing	4986 (84.57)	561 (80.72)	4425 (85.08)	0.0028
CAT score, mean±SD	19.30±6.94	18.53±6.81	19.41±6.95	0.0020
Acute exacerbation in the past 12 months, number (%)				
≥2 hospitalisation due to AECOPD	1442 (24.46)	162 (23.31)	1280 (24.61)	0.4535
≥1 emergency room visit due to AECOPD	2250 (38.16)	265 (38.13)	1985 (38.17)	0.9853
Laboratory finding, mean±SD				
pH	7.41±0.11	7.41±0.13	7.41±0.11	0.5058
PaO_2 (mm Hg)	78.41±26.82	79.62±27.27	78.26±26.76	<0.0001
$PaCO_2$ (mm Hg)	44.07±11.70	41.35±9.80	44.40±11.86	0.2709
Complication, number (%)				
Respiratory failure	1212 (20.56)	96 (13.81)	1116 (21.46)	<0.0001
Pulmonary heart disease	981 (16.64)	102 (14.68)	879 (16.90)	0.1392
Usage of medication during hospitalisation, number (%)				
Corticosteroid	4501 (76.34)	457 (65.76)	4044 (77.75)	<0.0001
Inhaled bronchodilator	4270 (72.42)	447 (64.32)	3823 (73.51)	<0.0001
Methylxanthines	4197 (71.18)	411 (59.14)	3786 (72.79)	<0.0001
Antibiotics	5212 (88.40)	581 (83.60)	4631 (89.04)	<0.0001
Respiratory support during hospitalisation, number (%)				<0.0001
Oxygen therapy	4543 (77.05)	450 (64.75)	4093 (78.70)	
Non-invasive positive-pressure ventilation	141 (2.39)	14 (2.01)	127 (2.44)	
Invasive positive-pressure ventilation	3 (0.05)	0 (0.00)	3 (0.06)	
ICU/RICU admission, number (%)	59 (1.00)	4 (0.58)	55 (1.06)	0.2299
Length of stay (days), median (quartile)	10 (8, 13)	10 (8, 13)	10 (8, 13)	0.0673
Total cost during hospitalisation (¥), median (quartile)	9211.90 (6657.39, 13067.21)	9125.35 (6280.45, 12917.24)	9221.02 (6711.27, 13078)	0.1868

AE, acute exacerbation; CAT, COPD assessment test; COPD, chronic obstructive pulmonary disease; ICU, intensive care unit; RICU, respiratory intensive care unit.

variable), sex (male/female), education (primary school and below, junior high school, and senior high school and above), smoking status (current, former and never), body mass index (BMI), airflow limitation severity (FEV_1%predicted), pre-existing comorbidities (asthma and cardiovascular diseases), COPD assessment test (CAT) score at admission, frequency of hospitalisation for AECOPD within the past year (<2 and ≥2), complications (respiratory failure) and treatments administered during the hospitalisation (corticosteroids, inhaled bronchodilators, methylxanthines, antibiotics and respiratory support). Comorbidities were determined based on the patient's history, symptoms and relevant examinations or former diagnoses in the medical records, including respiratory diseases (asthma), cardiovascular diseases (coronary heart disease, hypertension, pulmonary artery hypertension, heart failure and arrhythmia), digestive diseases (gastro-oesophageal reflux disease), and endocrine and metabolic diseases (diabetes and osteoporosis).

Statistical analysis

Descriptive statistics were calculated and stratified according to the groups (pre-COPD and COPD). Continuous variables are presented as mean±SD or median (quartiles), while categorical variables are presented as the number (percentage, %). Between-group differences were analysed using analysis of variance (Kruskal-Wallis test for skewed distribution) or the χ^2 test.

Time-to-event analyses were performed to assess lung function and clinical endpoints. The 30-day and 12-month incidence density rates of mortality and readmission as well as the 95% CIs were calculated based on

Table 3 Incidence density rates of mortality and readmission at 30 days and 12 months

	Overall		Pre-COPD		COPD		
	N/pm	IR (95% CI, per 1000 pm)	N/pm	IR (95% CI, per 1000 pm)	N/pm	IR (95% CI, per 1000 pm)	p value
After discharge at 30 days (30-day)							
All-cause mortality	9/4587	1.96 (0.68 to 3.24)	0/547	0.00 (0.00 to 8.70)	9/4040	2.23 (0.86 to 3.59)	0.6110
Respiratory-related mortality	3/4587	0.65 (0.00 to 1.39)	0/547	0.00 (0.00 to 8.70)	3/4040	0.74 (0.00 to 1.53)	0.9999
CHD-related mortality	3/4587	0.65 (0.00 to 1.39)	0/547	0.00 (0.00 to 8.70)	3/4040	0.74 (0.00 to 1.53)	0.9999
All-cause readmission	140/4519	30.98 (25.97 to 35.99)	18/537	33.52 (28.31 to 38.73)	122/3982	30.64 (25.65 to 35.63)	0.7175
Readmission with AE	114/4519	25.23 (20.69 to 29.76)	14/537	26.07 (21.46 to 30.68)	100/3982	25.11 (20.58 to 29.64)	0.8943
After discharge at 12 months (12 month)							
All-cause mortality	35/41 790	0.84 (0.00 to 1.67)	1/5037	0.20 (0.00 to 0.61)	34/36 753	0.93 (0.05 to 1.80)	0.1175
Respiratory-related mortality	18/41 790	0.43 (0.17 to 1.03)	0/5037	0.00 (0.00 to 0.80)	18/36 753	0.49 (0.00 to 1.13)	0.1557
CHD-related mortality	5/41 790	0.12 (0.20 to 0.44)	1/5037	0.20 (0.00 to 0.61)	4/36 753	0.11 (0.00 to 0.41)	0.9999
All-cause readmission	522/38 731	13.48 (10.14 to 16.81)	54/4700	11.49 (8.41 to 14.57)	468/34 031	13.75 (10.38 to 17.12)	0.2073
Readmission with AE	439/38 731	11.33 (8.27 to 14.40)	43/4700	9.15 (6.39 to 11.90)	396/34 031	11.64 (8.53 to 14.74)	0.1310

AE, acute exacerbation; CHD, coronary heart disease; COPD, chronic obstructive pulmonary disease; IR, incidence rate; N, number of events; pm, person-months.

the cumulative person-month follow-up for each category. The cumulative incidence function was used to generate the cumulative mortality and incidence of readmission curves.[18] The Fine-Grey subdistribution hazard model,[19] which simultaneously accounts for competing risk, was used to examine the association of lung function categories with risk of mortality and readmission, with adjustment for covariates.

All statistical analyses were performed using the SAS statistical software (V.9.4; SAS Institute, Cary, NC, USA). Statistical significance was set at p<0.05.

Patient and public involvement

None.

RESULTS

Baseline characteristics

We included 5896 patients from the ACURE study; among them, 695 participants were included in the pre-COPD group (figure 1). In the overall population, the mean age was 68.5 years (±9.62), and 76.68% of the patients were men. Compared with the COPD group, the pre-COPD group had a lower proportion of men (64.17% vs 78.35%, p<0.0001), a higher mean BMI (22.88±4.33 vs 22.35±3.81, p=0.0007) and fewer current and ex-smokers. The pre-COPD group had a significantly higher respiratory function than the COPD group (FEV_1% predicted, 68.4% vs 42.9%, p<0.0001). There was no significant between-group difference in the comorbidity profile; however, the pre-COPD group had fewer and more patients with asthma and coronary heart disease, respectively, than the COPD group (table 1).

Clinical characteristics of the populations

There was a significant between-group difference in the symptoms at admission. Generally, the pre-COPD group had milder symptoms, especially in sputum and wheezing, than the COPD group. The pre-COPD group had significantly lower CAT scores than the COPD group (18.53±6.81 vs 19.41±6.95, p=0.0020). During hospitalisation, the pre-COPD group had a lower occurrence of respiratory failure (13.81%) than the COPD group. There were no significant between-group differences in the complications of pulmonary heart disease. There was a significant between-group difference in the administered treatments, including drug therapy and respiratory support. Specifically, compared with the COPD group, the pre-COPD group had a lower proportion of patients who received corticosteroids, inhaled bronchodilators, methylxanthines, antibiotics or oxygen therapies. There were no significant between-group differences in the median length of hospital stay and total cost during hospitalisation (table 2).

Mortality and readmission after discharge

A total of 545 (9.2%) patients reported at least one outcome within a median follow-up duration of 271 days (274 and 270 days in the pre-COPD and COPD groups, respectively). At 30 days of follow-up, nine and zero patients in the COPD and pre-COPD groups, respectively, died; moreover, respiratory-related and cardiovascular-related mortality accounted for one-third of the total deaths. There were no significant between-group differences in the incidence rates of all-cause readmission after discharge (33.52/1000 and 30.64/1000 person-month in the pre-COPD and COPD groups, respectively,

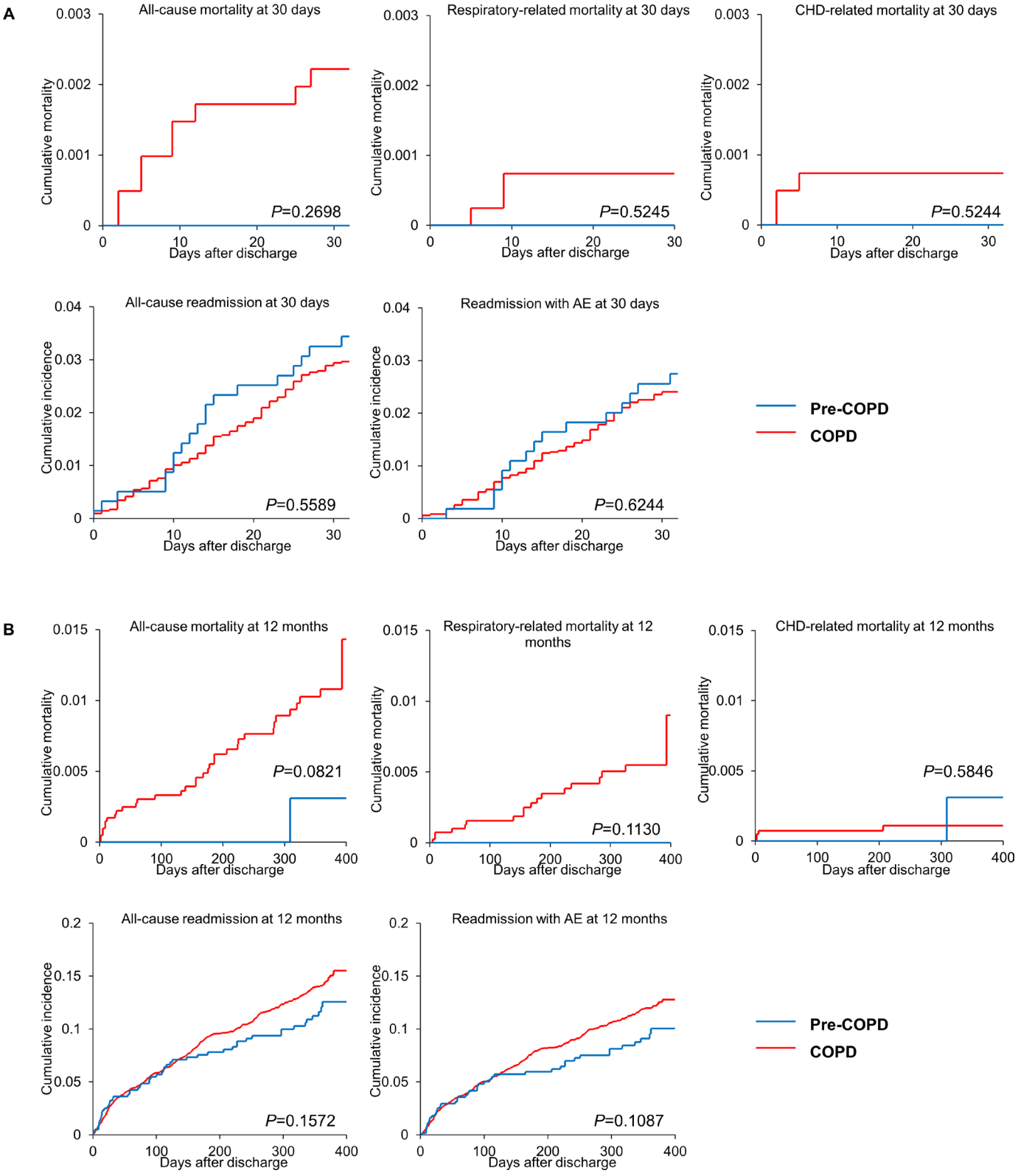

Figure 2 Cumulative mortality and incidence of readmission within (A) 30 days and (B) 12 months after hospital discharge. Cumulative incidence function was used to account for competing risks caused by death. AE, acute exacerbation; CHD, coronary heart disease; COPD, chronic obstructive pulmonary disease.

p=0.7175). AEs were the causes of approximately 80% of all readmissions.

The incidence density rates of readmission with AE were similar in both groups. At 12-month follow-up, 1 and 34 patients in the pre-COPD and COPD groups, respectively, died, with all-cause mortality rates of 0.20/1000 person-month and 0.93/1000 person-month (p=0.1175), respectively. The 12-month incidence density rates of

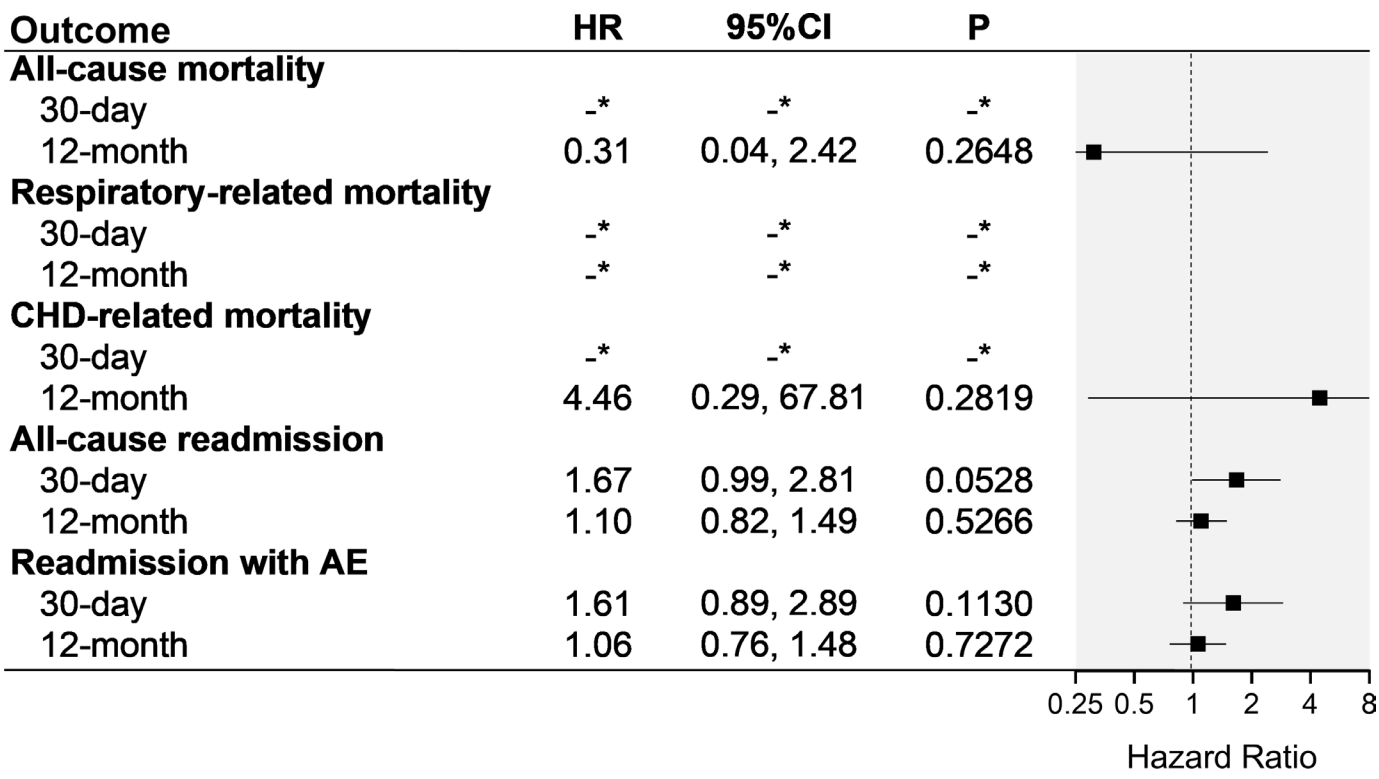

Figure 3 Association of lung function category (pre-COPD vs COPD) with 30-day and 12-month mortality and readmission. Models adjusted for age, sex, BMI, smoke, GOLD stage, CAT score, complication, medical history and medical treatment. *HR value cannot be estimated due to the small number of outcome events. AE, acute exacerbation; BMI, body mass index; CAT, COPD assessment test; COPD, chronic obstructive pulmonary disease.

all-cause readmission in the pre-COPD and COPD groups were 11.49/1000 person-month and 13.75/1000 person-month, respectively (p=0.2073), and 80% of them were AE-related. Table 3 shows the incidence rates of these outcomes.

Figure 2 illustrates the 30-day and 12-month cumulative mortality rates as well as the incidence of readmission in each group. There were no significant between-group differences in the cumulative rates of all cause-specific outcomes of interest (30-day all-cause mortality: 0% vs 0.2%, respiratory-related mortality: 0% vs 0.1%, CHD-related mortality: 0% vs 0.1%, all-cause readmission: 3.6% vs 3.2%, readmission with AE: 2.7% vs 2.4%; 12-month all-cause mortality: 0.3% vs 1.4%, respiratory-related mortality: 0% vs 0.9%, CHD-related mortality: 0.3% vs 0.1%, all-cause readmission: 12.6% vs 15.5% and readmission with AE: 10.0% vs 12.8%; p>0.05 for all).

In the multivariable models shown in figure 3, the lung function category was not significantly associated with 12-month all-cause mortality (HR, 95% CI 0.31, 0.04 to 2.42, p=0.2648) or cardiovascular-related mortality (HR, 95% CI 4.46, 0.29 to 67.81, p=0.2819), after adjusting for demographic and clinical characteristics in the Fine-Grey model. Moreover, the lung function category was not significantly correlated with all-cause readmission (30 days, HR, 95% CI 1.67, 0.99 to 2.81, p=0.0528; 12 months, HR, 95% CI 1.10, 0.82 to 1.49, p=0.5266) or AE-related readmission (30-day, HR, 95% CI 1.61, 0.89 to 2.89, p=0.1130; 12-month HR, 95% CI 1.06, 0.76 to 1.48, p=0.7272). The 30-day mortality and 12-month respiratory-related mortality could not be estimated due to a limited number of reported outcomes.

DISCUSSION

In our study, there was a small but notable proportion of patients with pre-COPD, which is characterised by respiratory symptoms without spirometrically confirmed airflow obstruction.[7] We observed no significant between-group differences in the risks of mortality, readmission and adverse cardiovascular and respiratory outcomes during the 30-day and 12-month follow-ups.

COPD is characterised by progressive airflow limitation, which eventually leads to respiratory symptoms and limited physical activity.[1 4] There is increasing interest in elucidating the pathogenesis of early-stage COPD, identifying individuals at risk of COPD and developing disease-modifying therapies.[7] Our findings indicate that the current spirometric criteria for COPD diagnosis may be inadequate for promptly identifying patients in the course of COPD.[20]

Since the risk of readmission and mortality did not differ between patients with pre-COPD and patients with COPD, it is important to detect respiratory changes compatible with a pre-COPD state. To further demonstrate this importance, other studies have reported that chronic respiratory symptoms and imaging abnormalities are very common in the earlier stages of COPD.

Inconsistent with our findings, a previous study found that patients with respiratory symptoms without spirometrically confirmed obstruction (ie, 70%≤FEV_1/FVC < 80%, GOLD 0) had an increased mortality risk compared with unobstructed individuals without symptoms.[21] Moreover, another study reported that the presence of chronic respiratory symptoms was associated with increased mortality (HR 1.35) among GOLD 0 patients.[22] Furthermore, the baseline Pi10, which is a CT measure of airway wall thickness, is positively associated with an increased risk of hospitalisation or mortality among patients with chronic lower respiratory disease without airflow obstruction.[23 24] Taken together, pre-COPD may be an indicator of future progression to fixed obstruction, and early interventions might change the disease trajectory.

Patients with COPD and airflow limitation commonly present comorbidities, including cardiovascular disease, metabolic syndrome, osteoporosis, digestive diseases, depression, anxiety and lung cancer.[25–27] These comorbidities not only affect prognosis but also influence mortality and 30-day all-cause readmission with AECOPD following the index hospitalisation.[28] Although the presence of comorbidities can significantly impact the course of COPD, we observed no significant between-group differences in the occurrence of comorbidities, except for asthma and coronary heart disease.

Given the lack of established definitions of asthma-COPD, there remain no clinical guidelines for the diagnosis of asthma-COPD. However, asthma-COPD, as a separate entity from COPD or asthma, is associated with a high frequency of respiratory symptoms and poor health status.[29 30]

Changes in the current socioeconomic status have led to an increase in the prevalence of coronary heart disease in the young 'at-risk' population,[31] which could be attributed to risk factors such as smoking, obesity and a sedentary lifestyle.[32] These factors may also contribute to the increasing prevalence of coronary heart disease among patients with pre-COPD. In our study, the prevalence of coronary disease was higher in the pre-COPD group than in the COPD group. Although there were no between-group differences in the risks of mortality and readmission during follow-up, the pre-COPD group had milder symptoms than the COPD group. Accordingly, patients with pre-COPD may have decreased self-management capacity and may benefit from interventions targeting smoking cessation, decision making, proactivity and seeking help. Therefore, comorbidities in patients with pre-COPD should be actively examined and routinely treated since they may influence mortality and hospitalisation. Circulating inflammatory mediators may initiate or worsen comorbidities, including ischaemic heart disease, heart failure and metabolic syndrome; however,[33] it remains unclear whether the association between coronary heart disease and pre-COPD is mediated through shared metabolic pathways or other systemic processes.

The present study provides an extensive description of the clinical features as well as short-term and long-term clinical outcomes of patients with pre-COPD in China. However, this study has several limitations. First, the ACURE only collected the frequency of severe AECOPD within the past year without moderate exacerbation history. Therefore, we could not assess the risk of exacerbation among patients; however, the occurrences of mild, moderate and severe AEs were prospectively recorded during follow-up. Second, given the limited follow-up duration, we could not investigate the relationship between pre-COPD and COPD development. Future studies on the risk of disease progression to COPD are warranted. Third, our findings demonstrated the relationship between baseline pre-COPD and prospective clinical outcomes but did not indicate whether distinct longitudinal trajectories within pre-COPD may be differentially associated with clinical outcomes.

CONCLUSION

Our findings suggest that patients with pre-COPD have mild respiratory symptoms and a similar profile as patients with COPD, including all-cause, respiratory disease-related and cardiovascular disease-related deaths as well as readmission within 30 days and 12 months after discharge. Further studies are warranted to explore the long-term changes in the disease trajectory of patients with pre-COPD through early interventions such as drug therapy and smoking cessation assistance, as well as their health status and socioeconomic burden.

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Acknowledgements The authors thank all the hospitals and staff who participated in the ACURE study for their help with data acquisition.

Contributors Conception and design: XR, YW, TY and CW. Data acquisition, analysis and interpretation: XR, YW, RH, FD, DL, TY and CW. Drafting of the manuscript and critical revision: XR, YW and TY. Accountability for work: XR, YW and TY. Guarantor: TY.

Funding This study was supported by the National High Level Hospital Clinical Research Funding, Elite Medical Professionals Project of China-Japan Friendship Hospital (No. ZRJY2021-TD02), the National Natural Science Foundation of China (No. 81800036), and the CAMS Innovation Fund for Medical Sciences (No. 2021-I2M-1-049).

Competing interests None declared.

Patient and public involvement Patients and/or the public were not involved in the design, conduct, reporting or dissemination plans of this research.

Patient consent for publication Not applicable.

Ethics approval We obtained approval from the Institutional Review Board of China-Japan Friendship Hospital (approval number 2015-88). Confidentiality and privacy of all the participants' information were maintained.

Provenance and peer review Not commissioned; externally peer reviewed.

Data availability statement Data are available upon reasonable request. The dataset and statistical codes are available from the authors upon request.

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