

# Impact of chronic lung disease after percutaneous coronary intervention in Japanese patients with acute coronary syndrome



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## KEYWORDS

- acute coronary syndrome
- chronic lung disease
- chronic obstructive pulmonary disease
- percutaneous coronary intervention

## Abstract

**Aims:** In Western countries, chronic lung disease (CLD) is a frequently encountered comorbidity in patients undergoing percutaneous coronary intervention (PCI). However, data are limited in Asians, where the prevalence of CLD is lower. We aimed to clarify the effects of CLD on in-hospital outcomes and discharge medications in ACS patients undergoing PCI in a multicentre registry.

**Methods and results:** We analysed 5,875 consecutive acute coronary syndrome patients undergoing PCI at 15 hospitals in Japan. Overall, 177 patients (3.0%) had CLD. The CLD patients were older, leaner, and had higher percentages of comorbidities. In-hospital mortality (7.3% vs. 3.8%,  $p=0.016$ ) and post-PCI cardiogenic shock (7.9% vs. 3.0%,  $p<0.001$ ) were higher in CLD patients; CLD was also an independent predictor of mortality after adjustment for baseline characteristics (OR 2.23;  $p=0.017$ ). In-hospital cardiac deaths were not significantly different in the two groups; however, in-hospital non-cardiac deaths were significantly higher in the CLD group (3.4% vs. 2.8%,  $p=0.624$ , 4.0% vs. 1.0%,  $p<0.001$ , respectively). Notably, prescription rates of beta-blockers (65.5% vs. 73.1%,  $p=0.041$ ) and statins (78.0% vs. 87.3%,  $p=0.049$ ) were lower in CLD patients. Further, in a subgroup of ST-elevation myocardial infarction patients, door-to-balloon time (DBT) was longer in CLD patients (113 vs. 97.9 min,  $p=0.016$ ), and CLD was an independent predictor of DBT >90 min (OR 3.05;  $p=0.002$ ).

**Conclusions:** CLD was associated with high in-hospital mortality, post-PCI cardiogenic shock, and low adherence to performance indicators in patients undergoing PCI in Japan. Clinical attention is needed, given the increasing numbers of PCI patients with pulmonary conditions.

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## Abbreviations

<b>ACS</b>	acute coronary syndrome
<b>CLD</b>	chronic lung disease
<b>COPD</b>	chronic obstructive pulmonary disease
<b>DBT</b>	door-to-balloon time
<b>JCD</b>	Japanese Cardiovascular Database
<b>NCDR</b>	National Cardiovascular Data Registry
<b>PCI</b>	percutaneous coronary intervention
<b>STEMI</b>	ST-elevation myocardial infarction

## Introduction

Chronic lung disease (CLD), including chronic obstructive pulmonary disease (COPD), chronic bronchitis, and emphysema, is a common comorbidity in coronary artery disease patients undergoing percutaneous coronary intervention (PCI). CLD and coronary artery disease share a common and significant risk factor: tobacco smoking. COPD is known to increase the risk of cardiovascular disease two- to threefold<sup>1,2</sup>. Systemic inflammation is present in patients with moderate-to-severe airflow obstruction and is associated with an increased risk of cardiac injury<sup>3</sup>. The World Health Organization stated that COPD is the fourth leading cause of mortality worldwide, and it could become the third leading cause by 2030.

The prevalence of CLD is lower in East Asian countries. Previous studies from Japan showed that CLD was present in only 2.4% of ischaemic heart disease patients<sup>4</sup>, which is comparatively low compared to Western studies (ranging from 6.0% to 13.9%)<sup>5,6</sup>. However, the prevalence of COPD continues to increase in Japan and in many Asian countries<sup>7</sup> due to increases in cigarette smoking, air pollution, and the ageing population. In Japan, CLD is currently the ninth cause of mortality but is not widely recognised as an important comorbidity in patients with ischaemic heart disease<sup>8</sup>.

However, the prognostic impact of CLD in acute coronary syndrome (ACS) has not been thoroughly investigated. Therefore, we aimed to clarify the effects of CLD on in-hospital mortality, post-procedural complications, and discharge medications in ACS patients undergoing PCI in a multicentre registry.

## Methods

The Japanese Cardiovascular Database (JCD) is a large, ongoing, multicentre prospective cohort study designed to collect clinical background and outcome data on PCI patients. Data pertaining to approximately 150 variables are being collected. Participating hospitals were instructed to record data from hospital visits for consecutive PCI patients and to register these data in an internet-based database. The database system performs checks to ensure that the reported data are complete and internally consistent. PCIs performed using any coronary devices may be included.

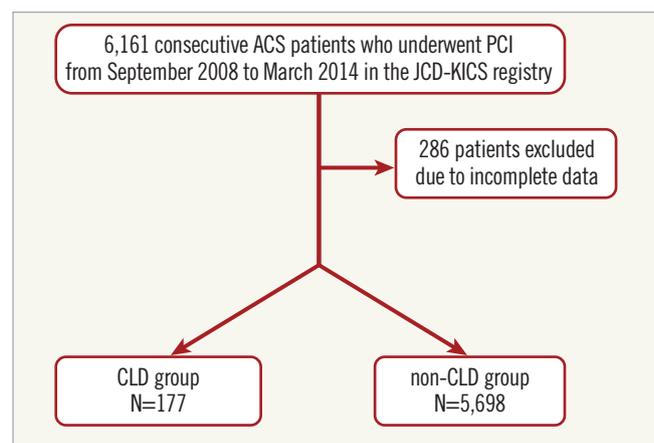
The decision to perform PCI is made according to the attending physician's clinical assessments; the study does not mandate specific interventional or surgical techniques, such as vascular access, or the use of a specific stent or closure device. The majority of the clinical variables in the JCD were defined according to the National Cardiovascular Data Registry (NCDR), sponsored by the American

College of Cardiology, to conduct comparative research and determine the factors which lead to disparities in PCI management<sup>9,10</sup>.

In this study, all 5,875 consecutive ACS patients who underwent PCI from September 2008 to March 2014 in 15 Japanese hospitals participating in the JCD were included (**Figure 1**). ACS was used to describe ST-elevation myocardial infarction (STEMI), non-ST-elevation myocardial infarction, and unstable angina. STEMI was defined as myocardial infarction with ST elevation<sup>9-11</sup>. For the present analysis, the ACS patients were divided into two groups, the CLD group and the non-CLD group, and we assessed the baseline characteristics and in-hospital mortality and complications after PCI. CLD was identified by the trained clinical research coordinators when one or more of the following criteria were met: 1) information on CLD status (COPD, chronic bronchitis, emphysema) was obtained in a medical chart review; 2) forced expiratory volume in one second/forced vital capacity <70% on spirometry<sup>12</sup>; or (3) current use of bronchodilators prior to PCI. This definition was consistent with that of the NCDR. If there were any inconsistencies in the medical records, the local site investigator and/or a primary investigator (S. Kohsaka or I. Ueda) made the final judgement. In Japan, unlike in other countries, COPD is diagnosed using spirometry<sup>13</sup>. Patients with asthma or seasonal allergies were not considered to have chronic lung disease.

In the subgroup of patients with STEMI, we investigated the door-to-balloon time (DBT) of 1,725 STEMI patients who arrived at hospital with symptoms for less than 12 hours. The DBT was defined as the time from initial arrival at the PCI facility to the first balloon inflation of the culprit artery. In this sub-analysis, we excluded patients with a DBT over 240 minutes and culprit lesions of >2 arteries and transfer patients from other hospitals who underwent PCI from all the STEMI patients. We excluded patients with a DBT >240 minutes because they presumably did not receive PCI as a primary reperfusion strategy. We excluded patients with >2 culprit arteries since multiple culprit arteries affected DBT.

The study endpoints included in-hospital mortality, heart failure, cardiogenic shock, and other complications. Complications were



**Figure 1.** Patient flow chart. JCD-KICS: Japan Cardiovascular Database-Keio Interhospital Cardiovascular Studies

defined as a composite endpoint of severe dissection or coronary perforation, myocardial infarction after PCI, cardiogenic shock or heart failure, cerebral bleeding or stroke, and bleeding complications. Bleeding complications were defined as those requiring transfusion, prolonging hospital stay, and/or causing a decrease in haemoglobin of >3.0 g/dl<sup>14</sup>. Further, bleeding complications were subdivided into puncture-site bleeding, retroperitoneal bleeding, gastrointestinal bleeding, genitourinary bleeding, or other bleeding.

### Statistical analysis

Continuous variables are expressed as means and standard deviations, and categorical variables are expressed as percentages. Continuous variables were compared using the Student's t-test, and differences between categorical variables were examined using a  $\chi^2$  test. Comparisons between groups were carried out with analysis of variance using general linear models. A multivariate logistic regression analysis was performed to determine the independent predictors of in-hospital mortality, in-hospital non-cardiac mortality and DBT >90 minutes for STEMI patients. Univariate logistic regression analysis was performed, and factors with a p-value <0.10 were included in the multivariate analysis. The covariates of univariate analysis for multivariate analysis were: female, previous myocardial infarction, previous heart failure, diabetes mellitus, diabetes mellitus with insulin, dialysis, cerebrovascular disease, peripheral artery disease, CLD, hypertension, cigarette smoking, dyslipidaemia, previous PCI, previous coronary bypass, cardiogenic shock at admission, cardiopulmonary arrest at admission, heart failure at admission, left main trunk stenosis, bifurcation lesion, type C lesion, STEMI, age >80, and BMI <21.6. All statistical calculations and analyses were performed using SPSS, Version 22 (IBM Corp., Armonk, NY, USA), and p-values <0.05 were considered statistically significant.

### Results

Of 5,875 ACS patients, 177 (3.0%) had CLD (**Figure 1**). The CLD patients were older and leaner than the non-CLD patients. Moreover, the CLD patients had a higher percentage of comorbidities, such as history of heart failure, cerebrovascular disease, peripheral artery disease, and heart failure symptoms on admission. Angiographically, the CLD group had a higher proportion of left main trunk stenosis and a lower proportion of three-vessel disease than the non-CLD group. The CLD group had a smaller proportion of STEMI patients than the non-CLD group; the two groups had similar incidences of cardiogenic shock on admission (**Table 1**).

The post-PCI complication rate was significantly higher in the CLD group than in the non-CLD group; moreover, incidences of in-hospital death and post-procedural cardiogenic shock were significantly higher in the CLD group than in the non-CLD group. Cardiac death rates were not significantly different between the two groups. However, non-cardiac deaths occurred more frequently in the CLD group than in the non-CLD group. Pulmonary-related and neurologically related deaths were significantly higher in the CLD group (**Table 2**). The results of the multivariable regression analysis

**Table 1. Baseline characteristics and procedural information.**

	Chronic lung disease group n=177 (%)	Non-chronic lung disease group n=5,698 (%)	p-value
Age, years	73.6±7.8	67.2±12.0	<0.001
Age >80	43 (24.3)	907 (15.9)	0.003
Female	23 (13.0)	1,262 (22.1)	0.004
Previous myocardial infarction	27 (15.3)	861 (15.1)	0.958
Previous heart failure	21 (11.9)	330 (5.8)	0.001
Diabetes mellitus	59 (33.3)	2,130 (37.4)	0.273
Diabetes mellitus with insulin	16 (9.0)	365 (6.4)	0.175
Dialysis	5 (2.8)	220 (3.9)	0.479
Cerebrovascular disease	29 (16.4)	468 (8.2)	<0.001
Peripheral artery disease	22 (12.4)	310 (5.4)	<0.001
Hypertension	130 (73.4)	4,074 (71.5)	0.572
Smoking	78 (44.1)	2,246 (39.4)	0.213
Dyslipidaemia	106 (59.9)	3,525 (61.9)	0.594
Previous percutaneous coronary intervention	43 (24.3)	1,109 (19.5)	0.111
Previous coronary bypass	6 (3.4)	207 (3.6)	0.865
Heart failure on admission	40 (22.6)	865 (15.2)	0.007
Cardiogenic shock on admission	11 (6.2)	433 (7.6)	0.493
Cardiopulmonary arrest on admission	5 (2.8)	254 (4.5)	0.297
Left main trunk stenosis	13 (7.3)	240 (4.2)	0.043
2-vessel disease	58 (32.8)	1,829 (32.1)	0.851
3-vessel disease	27 (15.3)	1,253 (22.0)	0.033
Bifurcation lesion	52 (29.4)	1,559 (27.4)	0.553
Type C lesion	47 (26.6)	1,545 (27.1)	0.869
Intra-aortic balloon pump	28 (15.8)	745 (13.1)	0.398
Before procedure insertion of intra-aortic balloon pump	5 (2.8)	144 (2.5)	0.804
During/after procedure insertion of intra-aortic balloon pump	23 (13.0)	620 (10.9)	0.375
Radial artery approach	51 (28.8)	1,459 (25.6)	0.336
ST-elevation myocardial infarction	75 (42.4)	2,859 (50.2)	0.041
Balloon angioplasty	24 (13.6)	674 (11.8)	0.483
Bare metal stent	48 (27.1)	1,568 (27.5)	0.907
Drug-eluting stent	104 (58.8)	3,388 (59.5)	0.851
Rotablator	3 (1.7)	58 (1.0)	0.382
Body mass index	22.7±3.2	24.0±3.7	<0.001

are shown in **Table 3**. After adjustment for differences in the baseline comorbidities, CLD was found to be an independent predictor of in-hospital mortality (odds ratio [OR] 2.23, confidence interval [CI]: 1.16-4.29, p=0.017), and non-cardiac in-hospital mortality (OR 3.50, CI: 1.48-8.30, p=0.004).

**Table 2. In-hospital mortality and complications, and discharge medications.**

	Chronic lung disease group n=177 (%)	Non-chronic lung disease group n=5,698 (%)	p-value
All complications	34 (19.2)	754 (13.2)	0.022
Coronary dissection	3 (1.7)	56 (1.0)	0.349
Coronary perforation	2 (1.1)	41 (0.7)	0.528
Myocardial infarction	2 (1.1)	102 (1.8)	0.512
Cardiogenic shock	14 (7.9)	172 (3.0)	<0.001
Heart failure	7 (4.0)	189 (3.3)	0.642
Cerebral infarction	1 (0.5)	30 (0.5)	0.945
Intracranial haemorrhage	0 (0)	5 (0.1)	0.693
Cardiac tamponade	0 (0)	30 (0.5)	0.333
Dialysis	1 (0.5)	110 (1.9)	0.189
Transfusion	9 (5.1)	214 (3.8)	0.362
Bleeding all	12 (6.8)	247 (4.3)	0.119
Puncture-site bleeding	3 (1.7)	65 (1.1)	0.497
Haematoma	0 (0)	51 (0.9)	0.206
Peritoneal bleeding	0 (0)	8 (0.1)	0.618
Gastrointestinal bleeding	2 (1.1)	36 (0.6)	0.416
Genitourinary bleeding	2 (1.1)	11 (0.2)	0.009
Other bleeding	7 (4.0)	112 (2.0)	0.064
In-hospital mortality	13 (7.3)	216 (3.8)	0.016
Cardiac causes	6 (3.4)	158 (2.8)	0.624
Non-cardiac causes	7 (4.0)	58 (1.0)	<0.001
Pulmonary causes	3 (1.7)	9 (0.2)	<0.001
Infectious causes	0 (0)	9 (0.2)	0.597
Nephrological causes	0 (0)	8 (0.1)	0.618
Neurological causes	1 (0.5)	2 (0.03)	0.002
Vascular causes	0 (0)	7 (0.1)	0.641
Other causes	3 (1.7)	23 (0.4)	0.011
Angiotensin-converting enzyme inhibitor or angiotensin receptor blocker prescription at discharge	115 (65.0)	3,930 (69.0)	0.378
Beta-blocker prescription at discharge	116 (65.5)	4,168 (73.1)	0.041
Statin prescription at discharge	138 (78.0)	4,974 (87.3)	0.049

Further, CLD significantly impaired performance indicators such as medications on discharge and DBT in STEMI patients. Prescription rates of beta-blockers and statins on discharge were lower in the CLD group. In the subgroup analysis of STEMI patients, DBT was longer in the CLD group than in the non-CLD group (113 vs. 97.9 min,  $p=0.016$ ). The clinical predictors of prolonged DBT are listed in **Table 4**. CLD was an independent predictor of DBT >90 min. In this subgroup analysis, CLD patients ( $N=43$ ) had higher mortality rates than non-CLD patients ( $N=1,682$ ; 11.6% vs. 4.9%,  $p=0.046$ ). CLD patients indeed tended

to have higher cardiac mortality rates than non-CLD patients (9.3% vs. 3.9%,  $p=0.072$ ). The rates of non-cardiac death in patients with versus without CLD were not significantly different (2.3% vs. 1.0%,  $p=0.402$ ). Furthermore, the proportion of patients with a DBT >90 min was significantly higher in the CLD group than in the non-CLD group (74.4% vs. 48.3%,  $p=0.001$ ). Importantly, the patients with a DBT >90 min had higher mortality rates than those with a DBT ≤90 min (6.5% vs. 3.6%,  $p=0.006$ ) and higher cardiac mortality rates (5.3% vs. 2.7%,  $p=0.006$ ), but not higher non-cardiac mortality rates (1.2% vs. 0.9%,  $p=0.575$ ).

## Discussion

Although CLD was observed in only 3% of the Japanese PCI patients in a contemporary multicentre registry, we showed that it is an independent risk factor for in-hospital mortality in ACS patients, even after adjustment for confounding factors by multivariate analysis. Importantly, CLD was associated with high in-hospital mortality, especially due to non-cardiac causes.

Of note, the CLD prevalence was 3% in our study, which is consistent with other previous registry studies in Japan<sup>4</sup> and East Asia<sup>15,16</sup>, and lower than that of ischaemic heart disease in Western countries (6.0%)<sup>5</sup>. Although pulmonary function tests were not mandated for all patients, this finding reflected real-world clinical practice. Since the prevalence of COPD may increase in Asian countries including Japan<sup>7</sup>, COPD could worsen the in-hospital outcomes of patients with ACS.

Our study is in agreement with previous studies reporting the prognosis of coronary artery disease patients with CLD. Nishiyama et al concluded that COPD was an independent risk factor for long-term cardiac and cardiovascular mortality in patients with ischaemic heart disease after revascularisation (PCI or coronary artery bypass grafting)<sup>4</sup>. Another study revealed that myocardial infarction patients with COPD showed a significantly high one-year mortality rate, although the revascularisation rate in COPD patients was about 40%<sup>5</sup>. However, data on the relative impact on the short-term outcomes of acute cardiac conditions such as ACS and the cause of death remain unclear. In our study, in-hospital mortality (7.3% vs. 3.8%,  $p=0.016$ ) was significantly higher in the CLD group than in the non-CLD group, and CLD was an independent predictor of in-hospital mortality after adjustment for baseline comorbidities (OR 2.23;  $p=0.017$ ).

In recent years, studies have focused on performance indicators for optimised therapy. Some of the performance indicators in ACS patients include the application of reperfusion therapy within 12 hrs, DBT in STEMI patients, optimal medications including beta-blockers, statins, and angiotensin-converting enzyme inhibitors or angiotensin receptor blockers, and antiplatelet therapy<sup>17</sup>. Optimal medications could improve in-hospital events<sup>18</sup>. Although the present study and a previous study<sup>19</sup> demonstrated that CLD could affect DBT for STEMI patients as well as the use of beta-blockers and statins, we were unable to show that key performance indicators could affect in-hospital cardiac mortality. We suspected that a prolonged DBT for CLD-STEMI patients could cause a significantly

**Table 3. Univariate and multivariate analysis for in-hospital mortality.**

Variable	Univariate		Multivariate	
	OR (CI)	p-value	OR (CI)	p-value
Female	1.22 (0.90-1.66)	0.197		
Previous myocardial infarction	1.31 (0.94-1.85)	0.114		
Previous heart failure	4.54 (3.23-6.38)	<0.001	2.56 (1.68-3.91)	<0.001
Diabetes mellitus	1.36 (1.07-1.82)	0.014	1.29 (0.93-1.81)	0.29
Diabetes mellitus with insulin	1.63 (1.05-2.54)	0.029	0.72 (0.40-1.30)	0.277
Dialysis	4.21 (2.80-6.35)	<0.001	5.23 (3.10-8.84)	<0.001
Cerebrovascular disease	2.33 (1.63-3.33)	<0.001	1.85 (1.22-2.80)	0.004
Peripheral artery disease	1.83 (1.16-2.88)	0.008	0.92 (0.54-1.57)	0.749
Chronic lung disease	2.01 (1.13-3.60)	0.016	2.23 (1.16-4.29)	0.017
Hypertension	0.94 (0.70-1.25)	0.668		
Smoking	0.680 (0.51-0.90)	0.007	0.84 (0.61-1.17)	0.312
Dyslipidaemia	0.44 (0.34-0.57)	<0.001	0.53 (0.39-0.72)	<0.001
Previous percutaneous coronary intervention	0.95 (0.67-1.33)	0.747		
Previous coronary bypass	1.50 (0.82-2.72)	0.182		
Cardiogenic shock at admission	14.1 (10.6-18.7)	<0.001	3.99 (2.64-6.04)	<0.001
Cardiopulmonary arrest at admission	14.5 (10.6-19.8)	<0.001	5.52 (3.46-8.80)	<0.001
Heart failure at admission	4.66 (3.55-6.12)	<0.001	2.47 (1.78-3.41)	<0.001
Left main trunk stenosis	5.03 (3.46-7.30)	<0.001	2.29 (1.44-3.64)	<0.001
3-vessel disease	1.61 (1.21-2.15)	0.001	1.25 (0.90-1.74)	0.190
Bifurcation lesion	1.15 (0.86-1.53)	0.348		
Type C lesion	1.97 (1.50-2.57)	<0.001	1.48 (1.08-2.02)	0.014
ST-elevation myocardial infarction	2.40 (1.80-3.20)	<0.001	2.19 (1.55-3.10)	<0.001
Age >80	2.94 (2.23-3.90)	<0.001	2.43 (1.71-3.44)	<0.001
BMI <21.6	2.03 (1.55-2.67)	<0.001	1.35 (0.98-1.87)	0.071

**Table 4. Multivariate analysis for door-to-balloon time >90 min in the subgroup analysis of ST-elevation myocardial infarction patients.**

Variable	Multivariate	
	OR (CI)	p-value
Women	1.13 (0.88-1.46)	0.330
Age >80	1.27 (0.94-1.71)	0.124
Previous percutaneous coronary intervention	1.77 (1.11-2.82)	0.017
Previous coronary bypass	2.07 (0.79-5.45)	0.139
Previous myocardial infarction	0.79 (0.49-1.28)	0.343
Previous heart failure	1.06 (0.59-1.92)	0.851
Diabetes mellitus	1.20 (0.96-1.51)	0.112
Diabetes mellitus with insulin	1.11 (0.63-1.96)	0.730
Hypertension	1.04 (0.85-1.28)	0.700
Smoker	0.89 (0.72-1.09)	0.260
Peripheral artery disease	1.66 (0.96-2.87)	0.072
Heart failure at admission	1.50 (1.11-2.01)	0.007
Intra-aortic balloon pump	1.12 (0.86-1.45)	0.391
Left main trunk stenosis	1.71 (0.67-4.38)	0.264
Type C lesion	1.14 (0.90-1.44)	0.278
Chronic lung disease	3.09 (1.53-6.25)	0.002

higher mortality rate and a trend towards a higher cardiac mortality rate; however, we could not definitively state that this would affect all CLD patients.

Previous studies investigated the reason why optimal medications were not prescribed<sup>20</sup>, and this was true even in our study. There is a concern that beta-blocker therapy may produce life-threatening bronchial constriction in COPD patients. In our study, a high rate of cardiogenic shock after PCI was another reason for the low prescription rate of beta-blockers. On the other hand, the reason for the low prescription rate of statins in CLD remains unclear. Statins have previously been shown to provide beneficial effects in COPD as well as ACS patients<sup>21,22</sup>.

Bronchial inflammation and elevated C-reactive protein levels are associated with an increased risk of cardiac injury<sup>3</sup> and play a role in plaque formation and rupture<sup>23</sup>. Hypoxia and increased work of breathing can worsen cardiac ischaemia and arrhythmia<sup>24</sup>. A previous study reported the incidence of cardiogenic shock after PCI in STEMI patients<sup>25</sup>. Wakabayashi et al speculated that left ventricular dysfunction might cause an increase in the right ventricular overload owing to hypoxia and pulmonary vasoconstriction. Therefore, pulmonary hypertension might have impaired systemic circulation in our patients as well. In our study, the CLD group had

a higher rate of cardiogenic shock after PCI, even though the complication rates and intra-aortic balloon pump insertion rates were similar between the groups. These burdens on the heart might be the reason for the high rates of cardiogenic shock. Man et al also showed that elevated C-reactive protein levels in COPD patients were associated with cardiovascular events including stroke<sup>26</sup>, and another study showed an association between inflammation in COPD patients and myocardial infarction and pneumonia<sup>27</sup>.

A higher in-hospital non-cardiac mortality rate was observed in the CLD group. Previous studies showed that COPD was an independent predictor of in-hospital non-cardiac death for heart failure patients<sup>28,29</sup>. Another study revealed that patients with ACS and a lower BMI had a higher proportion of COPD and a higher non-cardiac death rate<sup>30</sup>. However, to the best of our knowledge, no data have shown that COPD was an independent predictor of in-hospital non-cardiac death for patients with ACS who underwent PCI. Although we performed a multivariate logistic regression analysis to adjust for possible confounding variables, the heterogeneity of the CLD patients, such as lower BMI and higher age, may have affected the non-cardiac in-hospital mortality rate as shown in a previous study<sup>30</sup>, and we could not account for all confounding factors.

Despite the existence of confounding factors, we believe that the higher non-cardiac in-hospital mortality rate of CLD patients requires clinical attention. To prevent comorbidities, CLD patients need early cardiac rehabilitation, which is effective for acute myocardial infarction patients<sup>31</sup>, to avoid bed rest, and to increase their physical activity<sup>32</sup>. A previous report showed that transradial PCI could facilitate early rehabilitation for elderly patients with acute myocardial infarction<sup>33</sup> and might have a beneficial effect for CLD patients.

## Limitations

There were several limitations in this study. First, pulmonary function tests and interventional therapy for CLD were not performed in our study. In previous studies, the severity of COPD was a predictor of long-term mortality<sup>6</sup>; however, we could not investigate the relationship between the severity of CLD and in-hospital mortality. A previous study revealed that corticosteroid inhalation could reduce bronchial inflammation and ischaemic cardiac events<sup>34</sup>; however, this study did not include data on the use of corticosteroid inhalation therapy. Although pulmonary function tests were not mandated for all patients, our findings reflected real-world clinical practice. Second, we did not examine the symptoms in all patients. Diagnosis delay could not be calculated because of atypical presentations, which might be one of the reasons for a longer DBT in STEMI patients with CLD. Third, this analysis was performed on registered PCI patients, and therefore the ACS population without PCI was not investigated. It is possible that a portion of the CLD patients may not have been treated conservatively without PCI<sup>19</sup>, but, given the high percentage of an invasive strategy that is applied to ACS patients in Japan (97.2% of all STEMI patients underwent PCI in the J-AMI registry)<sup>35</sup>, the percentage of conservatively

treated patients was probably low. Finally, since we did not have post-PCI prescription rate data, we could not include beta-blockers in our multivariate analysis of in-hospital mortality.

## Conclusions

In conclusion, CLD is observed in 3% of Japanese ACS patients and should be recognised as a significant risk factor for in-hospital mortality and complications. Higher incidences of non-cardiac deaths might be the reasons for the poor prognosis of CLD. Clinical attention is needed, given the increasing number of PCI patients with multiple comorbidities including pulmonary conditions.

## Impact on daily practice

Although CLD prevalence was 3% in this contemporary PCI multicentre Japanese registry, it should be recognised as a significant risk factor for in-hospital mortality and morbidity. Higher incidences of non-cardiac deaths deserve clinical attention.

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## Conflict of interest statement

The authors have no conflicts of interest to declare.

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