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Original article

Body mass index and in-hospital mortality in patients with acute exacerbation of idiopathic pulmonary fibrosis

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Abstract

Background: Idiopathic pulmonary fibrosis (IPF) is an interstitial lung disease characterised by chronic fibrosis, and acute exacerbation of IPF (AE-IPF) is the leading cause of death in patients with IPF. Data on the association between the body mass index (BMI) and prognosis of AE-IPF are lacking. This study was performed to evaluate the association between the BMI and in-hospital mortality in patients who developed AE-IPF using a national inpatient database.

Methods: Using the Japanese Diagnosis Procedure Combination database, we retrospectively collected data of inpatients with AE-IPF from 1 July 2010 to 31 March 2018. We performed a multivariable logistic regression analysis to evaluate the association between all-cause in-hospital mortality and the BMI, categorised as underweight (<18.5 kg/m^2), low-normal weight (18.5–22.9 kg/m^2), high-normal weight (23.0–24.9 kg/m^2), overweight (25.0–29.9 kg/m^2), and obese (≥30.0 kg/m^2).

Results: In total, 14,783 patients were eligible for this study. The in-hospital mortality rate was 59.0%, 55.0%, 53.8%, 54.8%, and 46.0% in the underweight, low-normal weight, high-normal weight, overweight, and obese groups, respectively. Underweight patients had a significantly higher mortality rate (odds ratio, 1.25; 95% confidence interval, 1.10–1.42) and obese patients had a significantly lower mortality rate (odds ratio, 0.71; 95% confidence interval, 0.54–0.94) than low-normal weight patients.

Conclusion: Among patients with AE-IPF, the underweight group had higher mortality and the obese group had lower mortality.

Take home message: Among patients with acute exacerbation of idiopathic pulmonary fibrosis, the underweight group had higher mortality and the obese group had lower mortality.

Introduction

Patients with idiopathic pulmonary fibrosis (IPF), an interstitial lung disease characterised by chronic fibrosis, have a poor prognosis with an average survival time of 3 to 4 years [1]. A previous study showed that acute exacerbation of IPF (AE-IPF) was associated with high mortality with a mean survival time of less than 1 year and a 90-day mortality rate of approximately 50% after AE-IPF [2]. Risk factors for AE-IPF include oxygen administration, use of antacids, smoking, low lung function, a high serum Krebs von den Lungen-6 concentration, secondary pulmonary hypertension, and seasonality [3-5].

Generally, undernutrition is a potential prognostic factor in patients with respiratory diseases such as chronic obstructive pulmonary disease (COPD) [6] and pulmonary tuberculosis [7]. Moreover, protective effects of adipose tissue, referred to as the 'obesity paradox', are known in many chronic diseases including cardiovascular disease [8], chronic heart failure [9], and COPD [10]. In one study of patients with IPF, one-third of the patients were undernourished [11], and a lower body mass index (BMI) at the time of diagnosis has been proposed as a prognostic factor [12-16]. To the best of our knowledge, however, no study has focused on the association between the BMI and prognosis of AE-IPF.

The present study was performed to evaluate the association between the BMI and in-hospital mortality in patients who developed AE-IPF by using a nationwide inpatient database.

Patients and methods

Data source

Inpatient data were extracted from the Japanese Diagnosis Procedure Combination database, the details of which have been reported elsewhere [17]. More than 1,000 hospitals voluntarily contribute to the database, representing approximately 50% of all discharges from acute care hospitals in Japan. The data used in the present study included sex and age; body weight and height; smoking index; severity of dyspnoea based on the Hugh–Jones dyspnoea scale [18]; consciousness level on admission; intensive care unit (ICU) and/or emergency ward admission during hospitalisation; dates of hospitalisation and discharge; main diagnoses and pre-existing comorbidities on admission recoded by the attending physicians with the International Classification of Diseases, 10th revision (ICD-10) codes accompanied by text in Japanese; surgical and nonsurgical procedures and dates of the procedures performed; dates and doses of drugs administered during hospitalisation; and discharge status.

The Institutional Review Board of The University of Tokyo approved this study. The requirement for informed consent was waived because of the anonymous nature of the data.

Patient selection

This study used data from 1 July 2010 to 31 March 2018. The inclusion criteria were an age of ≥15 years, diagnosis of interstitial pneumonia (ICD-10 codes J84.1, J84.8, and J84.9), examination by computed tomography within 1 day after admission, and treatment with methylprednisolone at 500 to 1000 mg/day intravenously for 3 days starting within 4 days after admission [19]. Patients with IPF were selected as follows. First, patients with idiopathic interstitial pneumonias (IIPs) other than IPF, such as idiopathic nonspecific interstitial pneumonia, respiratory bronchiolitis-associated interstitial lung disease, cryptogenic organising pneumonia, acute interstitial pneumonia, desquamative interstitial pneumonia, lymphoid interstitial pneumonia, idiopathic pleuroparenchymal fibroelastosis, and unclassifiable idiopathic interstitial pneumonia, were excluded using the diagnoses in Japanese. Then, we excluded patients with the following secondary interstitial lung diseases identified using ICD-10 codes: hypersensitivity pneumonitis (J67), connective tissue disease associated with interstitial lung disease (M05, M06, and M30–35), sarcoidosis (D86), amyloidosis (E85), drug-induced lung disease (J70), radiation pneumonitis (J70), *Pneumocystis jirovecii* pneumonia (B59), pneumoconiosis (J60–65), pulmonary alveolar proteinosis (J84.0), eosinophilic pneumonia (J82), Langerhans cell histiocytosis (C96), and lymphangioleiomyomatosis (D21.9). We then excluded patients who received any of the following medications related to acute heart failure within 1 day after admission: furosemide, azosemide, carperitide, landiolol hydrochloride, digoxin, deslanoside, and tolvaptan [20]. We also excluded patients who underwent intra-aortic balloon pump therapy during hospitalisation. The remaining patients were assumed to have IPF. Finally, we excluded patients with missing data regarding consciousness and those who died within 4 days after admission.

Patient characteristics and BMI categories

The patient characteristics evaluated in this study were the BMI; age; sex; Hugh–Jones dyspnoea scale class on admission; consciousness on admission; smoking index; comorbidities; Charlson comorbidity index; surgical and nonsurgical procedures including tracheostomy, mechanical ventilation, and use of

medications for IPF during hospitalisation; and continuous renal replacement therapy within 1 day after admission. Consciousness on admission was evaluated using the Japan Coma Scale [21,22], which is widely used in Japan and has been shown to be well correlated with the Glasgow Coma Scale assessment [23]. The following comorbidities were identified using ICD-10 codes: lung cancer (C34), COPD (J44), pneumonia (J18), aspiration pneumonia (J69), pulmonary embolism (I26), chronic heart failure (I50), chronic renal failure (N18), and diabetes mellitus (E11). The Charlson comorbidity index was classified into five groups: 0, 1, 2, 3–5, and ≥6.

BMI categories were assigned based on the World Health Organization classifications of underweight (<18.5 kg/m^2), normal weight (18.5–24.9 kg/m^2), overweight (25.0–29.9 kg/m^2), and obese (≥30.0 kg/m^2) individuals. Normal weight was further divided into low-normal (18.5–22.9 kg/m^2) and high-normal (23.0–24.9 kg/m^2) [24,25].

Outcome

The primary outcome was all-cause in-hospital mortality.

Statistical analysis

Continuous variables are presented as mean ± standard deviation or median (interquartile range). The Kruskal–Wallis test was used to compare these variables between the groups. Proportions of categorical variables were compared using the chi-square test.

Missing data were observed for age, BMI, Hugh–Jones dyspnoea scale class, and smoking index. First, we performed a multiple imputation procedure to replace each missing value with a set of submitted plausible values using a Markov chain Monte Carlo algorithm known as imputation by chained equations [26], thereby creating 20 filled-in complete datasets. The multiple imputation method assumes that data are missing at random and that any systemic differences between the missing and observed values can be explained by differences in the observed data [27,28]. We then performed multivariable logistic regression analyses fitted with generalised estimating equations to estimate the odds ratio of in-hospital mortality for each BMI category. We defined the low-normal weight group as the reference category. Finally, the results of the multivariable logistic regression analyses from the 20 datasets were combined using Rubin's rule.

Second, we conducted a complete-case analysis that excluded all patients with missing data.

Multivariable logistic regression analysis for in-hospital mortality was performed to estimate the odds ratio for each BMI category with adjustment for other patient background factors while also adjusting for within-hospital clustering by means of a generalised estimating equation [29].

The threshold for significance was $P < 0.05$. All statistical analyses were performed using STATA/MP version 16 software (STATA Corp., College Station, TX, USA).

Results

During the study period, 95,221 patients underwent computed tomography within 1 day after admission and received high-dose methylprednisolone for 3 days starting within 4 days after admission (Figure 1). Among these 95,221 patients, 14,783 were eligible for this study. Their mean age was 75.0 ± 9.7 years, and the proportion of men was 71.7% (n = 10,594). Their mean BMI was 22.4 ± 3.7 kg/m^2, and 8,294 (56.1%) patients died during hospitalisation. The proportions of patients with missing data for age, BMI, Hugh–Jones dyspnoea scale class, and smoking index were 0.6% (n = 89), 11.0% (n = 1,629), 22.7% (n = 3,359), and 12.4% (n = 1,830) of all eligible patients, respectively.

The patient characteristics for each BMI category are shown in Table 1. The proportion of patients aged >80 years was higher in the underweight group but lower in the obese group. The proportion of females was higher in the underweight and obese groups. The proportion of patients with a poor level of consciousness on admission was higher in the underweight group than in the other groups. The proportion of patients with a Charlson comorbidity index of ≥6 was higher in the lower BMI groups. However, the obese group had the highest percentage of patients admitted to the ICU. The percentages of lung cancer and chronic renal failure were higher in the lower BMI categories. Conversely, the percentage of diabetes mellitus was higher in the higher BMI categories. The percentages of the following treatments and procedures were higher in the higher BMI categories: azithromycin, sulfamethoxazole trimethoprim, intravenous cyclophosphamide, cyclosporin, tacrolimus, pirfenidone, nintedanib, sivelestat sodium hydrate, and mechanical ventilation.

Figure 2 shows the all-cause in-hospital mortality rate for each BMI category. The in-hospital mortality rate was 59.0%, 55.0%, 53.8%, 54.8%, and 46.0% in the underweight, low-normal weight, high-normal weight, overweight, and obese groups, respectively.

Table 2 shows the results of the multivariable logistic regression analysis for all-cause in-hospital

mortality using the multiple imputation method for missing data. The mortality rate in the underweight group was significantly higher than that in the reference low-normal weight group (odds ratio, 1.25; 95% confidence interval, 1.10–1.42). In contrast, the mortality rate in the obese group was significantly lower than that in the reference low-normal weight group (odds ratio, 0.71; 95% confidence interval, 0.54–0.94). Older age, male sex, more severe dyspnoea scores, and a higher Charlson comorbidity index were significantly associated with higher mortality. In contrast, ICU admission, emergency unit admission, and care at an academic hospital were associated with lower mortality. With respect to comorbidities, lung cancer and chronic renal failure were associated with higher mortality, whereas COPD was associated with lower mortality. The following treatments and procedures were associated with higher mortality: intravenous or oral cyclophosphamide, cyclosporin, azathioprine, sivelestat sodium hydrate, thrombomodulin alfa, mechanical ventilation, and tracheotomy. In contrast, azithromycin and sulfamethoxazole trimethoprim were associated with lower mortality.

In the complete-case multivariable logistic regression analysis, the odds ratios (95% confidence intervals) with reference to the low-normal weight group were 1.25 (1.06–1.46), 0.94 (0.83–1.07), 1.01 (0.90–1.15), and 0.75 (0.54–0.94) for the underweight, high-normal weight, overweight, and obese groups, respectively.

Discussion

Using a nationwide inpatient database in Japan, we investigated the association between the BMI and mortality in patients with AE-IPF. Patients in the underweight group had a significantly higher mortality rate and those in the obese group had a significantly lower mortality rate than patients in the other weight groups. To our knowledge, the present study is the first to demonstrate relationship between the BMI and mortality in patients with AE-IPF.

Studies have been performed to evaluate the relationship between patients with IPF and body weight. A previous study showed that patients who lost ≥5% of body weight during the first year after diagnosis of IPF had a poorer prognosis than those who did not [12]. Moreover, staging based on annual body weight loss is reportedly a useful predictor of the prognosis of IPF [16]. These studies have suggested a detrimental impact of a lower BMI on patients with IPF, whereas other studies have, although indirectly, depicted a detrimental impact of obesity on patients with IPF. For example, one study showed that a

decline in the forced vital capacity was a prognostic factor for patients with IPF [30], but others showed that an increased BMI was associated with lower vital capacity [31] and forced vital capacity [32] in the general population. Data regarding the impact of the BMI on AE-IPF are inconsistent. One report indicated that the BMI was not a risk factor for developing AE [4], whereas another study showed that a high BMI was a risk factor for developing AE [33]. To our knowledge, however, no previous study has examined the relationship between the BMI and mortality in patients with AE-IPF. The in-hospital mortality rate for all patients with AE-IPF s in the current study was 56.1%, which is similar to previously reported rates [2]. The underweight group had the highest mortality rate and the obese group had the lowest. A British database study demonstrated that the association between BMI and mortality varied among diseases [34]. Some diseases had a J-shaped association with BMI and other diseases had an inverse linear association with BMI. The results of our study were similar to the association between BMI and mortality of lung cancer in that study. Obesity may be a risk factor for developing AE-IPF, but it may be favourable in patients who developed AE-IPF. The mechanism by which obese patients with AE-IPF have favourable outcomes remains unknown.

The BMI can be influenced by a patient's background factors, such as ethnic characteristics. Reports have suggested that Asian ethnic populations have different associations between the BMI and health risks than Western populations [35]. Additionally, Asian ethnic populations generally have a higher percentage of body fat than Caucasians of the same age, sex, and BMI, which may contribute to the difference in the properties of fat, including adipocytokines such as adiponectin, leptin, and resistin [35,36]. The BMI of patients with IPF in the present Japanese study was lower than that reported from other countries [14]. Such a difference in the BMI distribution between Asian and Caucasian patients with IPF has been observed in previous studies [15,37,38]. The association between the BMI and prognosis in patients with AE-IPF may therefore vary among different ethnic groups.

Several limitations of this study should be acknowledged. Because the database does not include data on laboratory examinations, pulmonary function tests, performance status, and radiological findings, the diagnosis and severity of IPF could not be precisely evaluated in this study. Additionally, the accuracy of the IPF diagnosis was not confirmed by radiological and pathological analyses because we based the diagnosis of IPF on physician-diagnosed IPF. To classify IPF, all cases of IIPs other than IPF and secondary interstitial pneumonia were excluded using the diagnoses in Japanese or ICD-10 codes, because

the specificity of diagnoses in the DPC data are high in general [39].

In conclusion, this study has demonstrated that the underweight group had higher mortality and the obese group had lower mortality in patients with AE-IPF.

Author contributions

N. Awano designed the study, analysed and interpreted the data, and prepared the manuscript. T. Jo designed the study, analysed and interpreted the data, and prepared the manuscript. H. Yasunaga analysed and interpreted the data and prepared the manuscript. M. Inomata interpreted the data. N. Kuse interpreted the data. M. Tone interpreted the data. K. Morita collected and interpreted the data. H. Matsui collected the data. K. Fushimi collected the data. T. Nagase interpreted the data and prepared the manuscript. T. Izumo interpreted the data and prepared the manuscript. All authors approved the final manuscript.

Support statement

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Conflict of interest

N. Awano has nothing to disclose. T. Jo has nothing to disclose. H. Yasunaga reports receiving grants from the Ministry of Health, Labour and Welfare, Japan and the Ministry of Education, Culture, Sports, Science and Technology, Japan during the conduct of the study. M. Inomata has nothing to disclose. N. Kuse has nothing to disclose. M. Tone has nothing to disclose. K. Morita has nothing to disclose. H. Matsui has nothing to disclose. K. Fushimi has nothing to disclose. T. Nagase has nothing to disclose. T. Izumo has nothing to disclose.

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Table 1. Patients' characteristics and comorbidities in relation to body mass index category

	Body mass index (kg/m^2)						
	Underweight <18.5 kg/m^2 (n = 1781)	Low-normal weight 18.5–22.9 kg/m^2 (n = 5931)	High-normal weight 23.0–24.9 kg/m^2 (n = 2669)	Overweight 25.0–29.9 kg/m^2 (n = 2399)	Obese ≥30 kg/m^2 (n = 374)	Missing (n = 1629)	*P*-value *
Age, years							
15–60	89 (5.0)	315 (5.3)	159 (6.0)	185 (7.7)	83 (22.2)	82 (5.0)	<0.001
61–70	353 (19.8)	1191 (20.1)	661 (24.8)	617 (25.7)	93 (24.9)	273 (16.8)	
71–80	693 (38.9)	2475 (41.7)	1163 (43.6)	1039 (43.3)	134 (35.8)	657 (40.3)	
≥81	639 (35.9)	1913 (32.3)	676 (25.3)	550 (22.9)	46 (12.3)	608 (37.3)	
Missing	7 (0.4)	37 (0.6)	10 (0.4)	8 (0.3)	18 (4.8)	9 (0.6)	
Sex							<0.001
Male	1028 (57.7)	4344 (73.2)	2113 (79.2)	1791 (74.7)	223 (59.6)	1095 (67.2)	
Female	753 (42.3)	1587 (26.8)	556 (20.8)	608 (25.3)	151 (40.4)	534 (32.8)	
Hugh-Jones dyspnoea class							<0.001
1	72 (4.0)	309 (5.2)	144 (5.4)	136 (5.7)	26 (7.0)	57 (3.5)	
2	93 (5.2)	411 (6.9)	208 (7.8)	192 (8.0)	29 (7.8)	78 (4.8)	
3	120 (6.7)	466 (7.9)	231 (8.7)	208 (8.7)	30 (8.0)	82 (5.0)	

4	296 (16.6)	1057 (17.8)	513 (19.2)	444 (18.5)	61 (16.3)	240 (14.7)	
5	701 (39.4)	2358 (39.8)	1029 (38.6)	928 (38.7)	156 (41.7)	749 (46.0)	
Missing	499 (28.0)	1330 (22.4)	544 (20.4)	491 (20.5)	72 (19.3)	423 (26.0)	
Japan coma scale score							<0.001
0-digit (alert)	1484 (83.3)	5208 (87.8)	2432 (91.1)	2176 (90.7)	344 (92.0)	1329 (81.6)	
1-digit (dull)	219 (12.3)	565 (9.5)	186 (7.0)	177 (7.4)	24 (6.4)	232 (14.2)	
2- or 3-digit (somnolence or coma)	78 (4.4)	158 (2.7)	51 (1.9)	46 (1.9)	6 (1.6)	68 (4.2)	
Charlson comorbidity index							<0.001
0	870 (48.9)	2962 (49.9)	1380 (51.7)	1254 (52.3)	225 (60.2)	952 (58.4)	
1	235 (13.2)	788 (13.3)	358 (13.4)	342 (14.3)	52 (13.9)	204 (12.5)	
2	401 (22.5)	1316 (22.2)	588 (22.0)	495 (20.6)	59 (15.8)	311 (19.1)	
3–5	153 (8.6)	508 (8.6)	198 (7.4)	209 (8.7)	23 (6.2)	104 (6.4)	
≥6	122 (6.9)	357 (6.0)	145 (5.4)	99 (4.1)	15 (4.0)	58 (3.6)	
Smoking index, pack-years							<0.001
0	977 (54.9)	2587 (43.6)	1062 (39.8)	934 (38.9)	163 (43.6)	705 (43.3)	
1–19	105 (5.9)	425 (7.2)	196 (7.3)	156 (6.5)	23 (6.2)	101 (6.2)	
20–39	201 (11.3)	764 (12.9)	346 (13.0)	351 (14.6)	49 (13.1)	150 (9.2)	

40–59	182 (10.2)	830 (14.0)	422 (15.8)	354 (14.8)	42 (11.2)	163 (10.0)	
≥60	134 (7.5)	648 (10.9)	351 (13.2)	343 (14.3)	44 (11.8)	145 (8.9)	
Missing	182 (10.2)	677 (11.4)	292 (10.9)	261 (10.9)	53 (14.2)	365 (22.4)	
Intensive care unit admission	223 (12.5)	812 (13.7)	371 (13.9)	358 (14.9)	73 (19.5)	204 (12.5)	0.004
Emergency unit admission	185 (10.4)	650 (11.0)	285 (10.7)	259 (10.8)	37 (9.9)	167 (10.3)	0.943
Academic hospital	1351 (75.9)	4728 (79.7)	2142 (80.3)	1947 (81.2)	306 (81.8)	1395 (85.6)	<0.001
Hospital length of stay, days	25 (14–44)	25 (14–42)	24 (14–41)	24 (14–41)	25.5 (15–42)	21 (12–39)	0.259 †
Lung cancer	208 (11.7)	793 (13.4)	383 (14.3)	288 (12.0)	28 (7.5)	137 (8.4)	<0.001
COPD	88 (4.9)	312 (5.3)	129 (4.8)	117 (4.9)	20 (5.3)	74 (4.5)	0.863
Chronic heart disease	196 (11.0)	617 (10.4)	245 (9.2)	280 (11.7)	40 (10.7)	186 (11.4)	0.067
Chronic renal failure	74 (4.2)	216 (3.6)	72 (2.7)	63 (2.6)	6 (1.6)	34 (2.1)	<0.001
Diabetes mellitus	332 (18.6)	1421 (24.0)	725 (27.2)	697 (29.1)	147 (39.3)	370 (22.7)	<0.001
Pneumonia	128 (7.2)	378 (6.4)	191 (7.2)	144 (6.0)	31 (8.3)	123 (7.6)	0.169
Pulmonary embolism	9 (0.5)	30 (0.5)	16 (0.6)	12 (0.5)	1 (0.3)	6 (0.4)	0.912
Noradrenaline	50 (2.8)	165 (2.8)	70 (2.6)	68 (2.8)	15 (4.0)	45 (2.8)	0.799
Azithromycin	242 (13.6)	921 (15.5)	402 (15.1)	380 (15.8)	56 (15.0)	210 (12.9)	0.049
Sulfamethoxazole trimethoprim	966 (54.2)	3620 (61.0)	1680 (62.9)	1567 (65.3)	228 (61.0)	876 (53.8)	<0.001
Cyclophosphamide (intravenous)	113 (6.3)	614 (10.4)	351 (13.2)	375 (15.6)	56 (15.0)	182 (11.2)	<0.001

Cyclophosphamide (oral)	25 (1.4)	93 (1.6)	43 (1.6)	42 (1.8)	6 (1.6)	16 (1.0)	0.492
Cyclosporin	138 (7.7)	631 (10.6)	338 (12.7)	345 (14.4)	50 (13.4)	152 (9.3)	<0.001
Tacrolimus	26 (1.5)	115 (1.9)	49 (1.8)	64 (2.7)	12 (3.2)	15 (0.9)	0.001
Azathioprine	18 (1.0)	101 (1.7)	57 (2.1)	46 (1.9)	5 (1.3)	25 (1.5)	0.097
Pirfenidone	68 (3.8)	265 (4.5)	111 (4.2)	152 (6.3)	23 (6.1)	59 (3.6)	<0.001
Nintedanib	21 (1.2)	97 (1.6)	53 (2.0)	47 (2.0)	10 (2.7)	11 (0.7)	0.003
Sivelestat sodium hydrate	182 (10.2)	801 (13.5)	394 (14.8)	379 (15.8)	60 (16.0)	264 (16.2)	<0.001
Thrombomodulin alfa	106 (6.0)	357 (6.0)	170 (6.4)	157 (6.5)	26 (7.0)	95 (5.8)	0.868
Mechanical ventilation	425 (23.9)	1619 (27.3)	787 (29.5)	751 (31.3)	134 (35.8)	500 (30.7)	<0.001
Haemodialysis	31 (1.7)	82 (1.4)	28 (1.0)	28 (1.2)	3 (0.8)	19 (1.2)	0.344
Tracheotomy	57 (3.2)	183 (3.1)	86 (3.2)	67 (2.8)	19 (5.1)	47 (2.9)	0.299

Continuous variables are shown as number (%) or median (interquartile range).

COPD, chronic obstructive pulmonary disease.

*All *P*-values obtained by chi-square test except hospital length of stay (†Kruskal–Wallis test).

Table 2. Multivariable logistic regression analysis for all-cause in-hospital mortality

	Adjusted OR	95% CI	*P*-value
Body mass index, kg/m^2			
<18.5	1.25	1.10–1.42	0.001
18.5–22.9	Reference		
23.0–24.9	0.92	0.82–1.02	0.122
25.0–29.9	0.98	0.88–1.09	0.706
≥30.0	0.71	0.54–0.94	0.016
Age, years			
15–60	Reference		
61–70	1.86	1.55–2.29	<0.001
71–80	2.32	1.94–2.77	<0.001
≥81	2.98	2.47–3.59	<0.001
Sex			
Female	Reference		
Male	1.37	1.23–1.53	<0.001
Hugh-Jones dyspnoea class			
1	Reference		
2	1.20	0.94–1.52	0.137
3	1.41	1.12–1.78	0.003
4	2.02	1.62–2.51	<0.001
5	4.91	4.02–6.01	<0.001
Japan coma scale score			
0-digit (alert)	Reference		
1-digit (dull)	1.19	1.02–1.39	0.024
2- or 3-digit (somnolence or coma)	0.97	0.73–1.29	0.822
Charlson comorbidity index			
0	Reference		

1	0.87	0.77–0.98	0.027
2	1.23	1.09–1.38	0.001
3–5	1.06	0.89–1.28	0.503
≥6	2.60	2.12–3.19	<0.001
Smoking index, pack-years			
0	Reference		
1–20	0.84	0.72–0.98	0.026
20–40	0.82	0.73–0.93	0.002
40–60	0.77	0.67–0.89	<0.001
≥60	0.78	0.68–0.90	0.001
Intensive care unit admission	0.78	0.67–0.91	0.001
Emergency unit admission	0.79	0.67–0.94	0.007
Academic hospital	0.70	0.63–0.78	<0.001
Lung cancer	2.28	1.94–2.69	<0.001
COPD	0.77	0.63–0.94	0.010
Chronic heart disease	1.05	0.91–1.22	0.484
Chronic renal failure	1.65	1.26–2.16	<0.001
Diabetes mellitus	0.94	0.85–1.03	0.177
Pneumonia	0.97	0.81–1.16	0.724
Pulmonary embolism	0.83	0.48–1.45	0.516
Noradrenaline	0.80	0.62–1.03	0.084
Azithromycin	0.79	0.69–0.89	0.001
Sulfamethoxazole trimethoprim	0.42	0.39–0.46	<0.001
Cyclophosphamide (intravenous)	4.20	3.59–4.91	<0.001
Cyclophosphamide (oral)	2.84	1.99–4.06	<0.001
Cyclosporin	2.31	1.99–2.68	<0.001
Tacrolimus	0.89	0.64–1.22	0.688
Azathioprine	1.77	1.21–2.60	0.003

Pirfenidone	1.13	0.93–1.39	0.223
Nintedanib	0.76	0.57–1.01	0.063
Sivelestat sodium hydrate	1.33	1.13–1.55	<0.001
Thrombomodulin alfa	3.07	2.35–4.01	<0.001
Mechanical ventilation	4.01	3.54–4.53	<0.001
Haemodialysis	1.26	0.81–1.96	0.305
Tracheotomy	1.82	1.30–2.54	<0.001

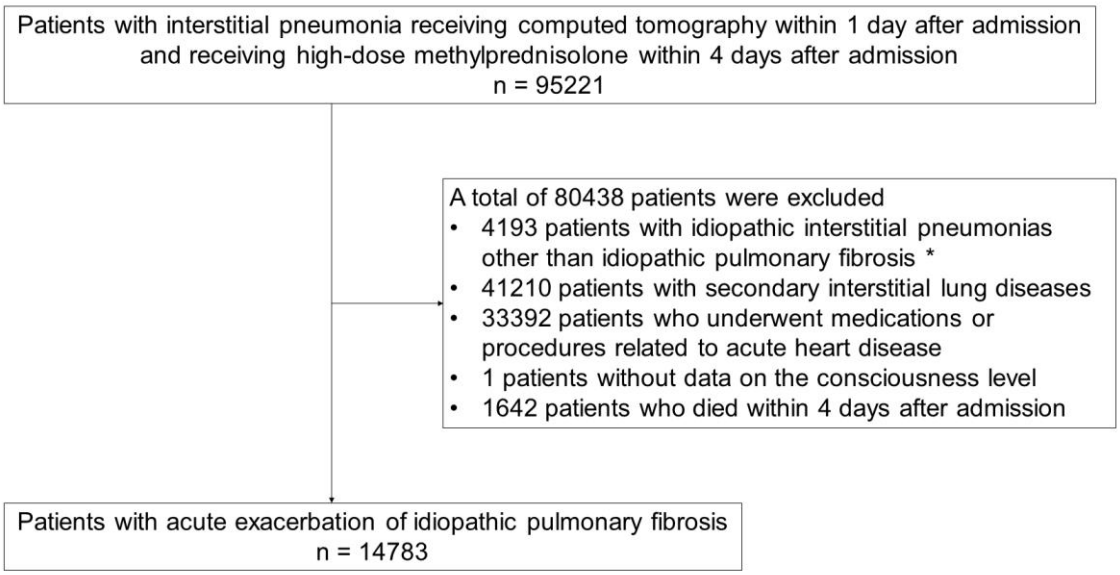
OR, odds ratio; CI, confidence interval; COPD, chronic obstructive pulmonary disease.

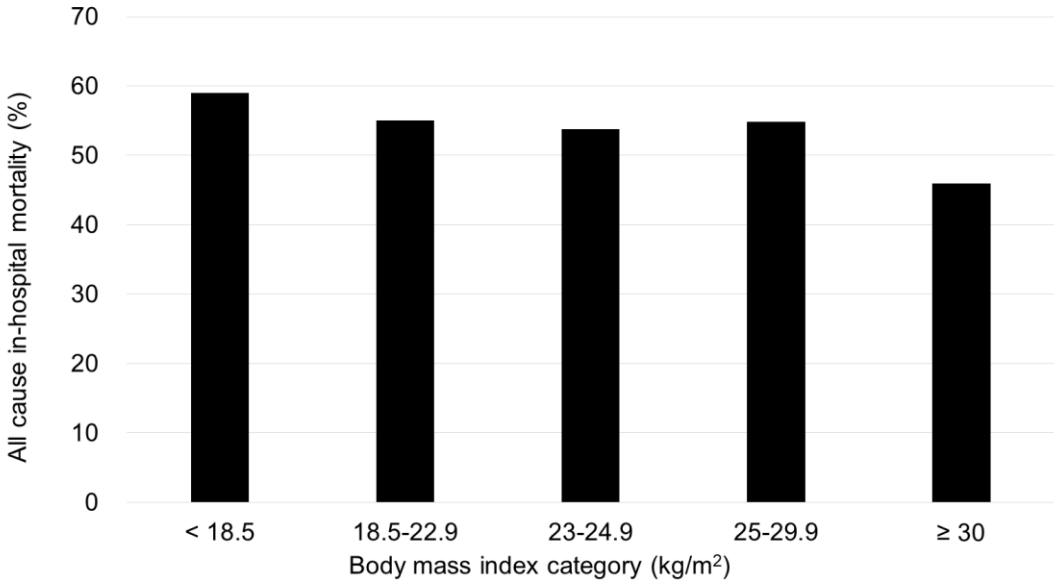
Figure Legends

Figure 1. Flow chart of patient selection.

* idiopathic nonspecific interstitial pneumonia, respiratory bronchiolitis-associated interstitial lung disease, cryptogenic organising pneumonia, acute interstitial pneumonia, desquamative interstitial pneumonia, lymphoid interstitial pneumonia, idiopathic pleuroparenchymal fibroelastosis, and unclassifiable idiopathic interstitial pneumonia.

Figure 2. All cause in-hospital mortality in patients with acute exacerbation of idiopathic pulmonary fibrosis in relation to body mass index category.


Patients with interstitial pneumonia receiving computed tomography within 1 day after admission and receiving high-dose methylprednisolone within 4 days after admission
n = 95221
A total of 80438 patients were excluded
• 4193 patients with idiopathic interstitial pneumonias other than idiopathic pulmonary fibrosis *
• 41210 patients with secondary interstitial lung diseases
• 33392 patients who underwent medications or procedures related to acute heart disease
• 1 patients without data on the consciousness level
• 1642 patients who died within 4 days after admission
Patients with acute exacerbation of idiopathic pulmonary fibrosis
n = 14783


70
60
50
40
30
20
10
0
All cause in-hospital mortality (%)
< 18.5
18.5-22.9
23-24.9
25-29.9
≥ 30
Body mass index category (kg/m2)