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Original Article

Impact of prior pulmonary tuberculosis in treatment outcomes of HCAP and CAP patients in intensive care units

Fan-Min Lin [a,1], Jia-Yih Feng [b,c,d,1], Wen-Feng Fang [e,f], Chieh-Liang Wu [g], Chong-Jen Yu [h,i], Meng-Chih Lin [e,f], Shih-Chi Ku [h], Chang-Wen Chen [j], Chih-Yen Tu [k,l], Kuang-Yao Yang [b,m,*]

[a] *Division of Pulmonary Medicine, Department of Internal Medicine, Kaohsiung Armed Forces General Hospital, Kaohsiung, Taiwan*
[b] *Department of Chest Medicine, Taipei Veterans General Hospital, Taipei, Taiwan*
[c] *Institute of Clinical Medicine, School of Medicine, National Yang-Ming University, Taipei, Taiwan*
[d] *School of Medicine, National Yang-Ming University, Taipei, Taiwan*
[e] *Division of Pulmonary and Critical Care Medicine and Department of Respiratory Therapy, Kaohsiung Chang Gung Memorial Hospital and Chang Gung University College of Medicine, Kaohsiung, Taiwan*
[f] *Department of Respiratory Care, Chang Gung University of Science and Technology, Chiayi, Taiwan*
[g] *Center for Quality Management, Taichung Veterans General Hospital, Taichung, Taiwan*
[h] *Department of Internal Medicine, National Taiwan University Hospital, Taipei, Taiwan*
[i] *College of Medicine, National Taiwan University, Taipei, Taiwan*
[j] *Medical Intensive Care Unit, Department of Internal Medicine, National Cheng-Kung University Hospital, Tainan, Taiwan*
[k] *Division of Pulmonary and Critical Care Medicine, Department of Internal Medicine, China Medical University Hospital, Taichung, Taiwan*
[l] *School of medicine, China Medical University, Taichung, Taiwan*
[m] *Institute of Emergency and Critical Care Medicine, School of Medicine, National Yang-Ming University, Taipei, Taiwan*

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Abstract *Background/purpose:* It is controversial whether healthcare-associated pneumonia (HCAP) belongs to a unique clinical entity or it shares common characteristics with community-acquired pneumonia (CAP). The impact of prior pulmonary tuberculosis (PTB) in clinical

* Corresponding author. Department of Chest Medicine, Taipei Veterans General Hospital, No.201, Sec. 2, Beitou Rd., Beitou Dist., Taipei City 112, Taiwan. Fax: +886 2 28752380.
E-mail address: kyyang@vghtpe.gov.tw (K.-Y. Yang).
[1] Fan-Min Lin and Jia-Yih Feng contributed equally.

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Healthcare-associated pneumonia;
Intensive care unit;
Mortality;
Tuberculosis

presentation and treatment outcome of ICU-admitted CAP and HCAP patients also remains unknown.
Methods: We report a nationwide, multi-center, retrospective study. ICU-admitted CAP and HCAP patients from six medical centers in Taiwan were enrolled for analysis. Patients were defined as either CAP or HCAP cases, and with and without prior PTB, according to the database of Taiwan CDC. The disease severity, microbiologic characteristics, and treatment outcomes between CAP and HCAP patients with or without prior PTB were compared and analyzed.
Results: A total of 414 ICU-admitted patients, including 176 CAP cases and 238 HCAP cases were included for analysis during the study period. In both CAP and HCAP subgroups, the pneumonia severities, proportions of organ dysfunction, and microbiologic characteristics were similar between patients with and without prior PTB. In survival analysis, patients with prior PTB had higher 30-day mortality than those without prior PTB (38.9% vs. 16.5%, $p = 0.021$) in the CAP population. Multivariate analysis revealed that a history of prior PTB was an independent clinical factor associated with higher 30-day mortality rate in CAP patients (HR = 4.45, 95% CI: 1.81–10.98, P = 0.001).
Conclusion: History of prior PTB is an independent clinical factor for increased 30-day mortality rate in ICU-admitted CAP patients, but not in ICU-admitted HCAP patients.

Introduction

Healthcare-associated pneumonia (HCAP) is a special category of pneumonia that occurs in patients who had contact with or previous exposure to a healthcare facility.[1] Previously, HCAP was considered to be a specific entity its unique microbiological characteristics and treatment outcomes.[2] However, the concept of HCAP has been recently challenged and the disease was removed from the current hospital-acquired pneumonia (HAP)/ventilator-associated pneumonia (VAP) guidelines.[3] It remains controversial whether HCAP is indeed a separate clinical entity, or whether it is simply a subgroup of community-acquired pneumonia (CAP).

Tuberculosis (TB) is the deadliest infection worldwide. It is transmitted via airborne particles, and the on treatment mortality among active TB patients ranged from 5% to 30% in previous reports.[4–6] CAP caused by *Mycobacterium tuberculosis* is common in TB-endemic areas.[7] Commonly used antibiotics in CAP, especially fluoroquinolone,[8] may potentially mask the diagnosis of pulmonary TB. Concomitant TB in patients with HCAP has also been reported in our previous study.[9] It is estimated that 1%–3% patients with active TB require intensive care due to respiratory failure, development of multi-organ failures, or occurrence of acute respiratory distress syndromes.[10–13] The in-hospital mortality among TB patients with intensive care unit (ICU) admission ranges from 38% to 59%,[14–16] which is much higher than that in patients with severe pneumonia and respiratory failure.[17] The high mortality rate of ICU-admitted patients with TB originates from high illness severity, malnutrition, presence of organ failure, extensiveness of lung destruction, and delay in treatment initiation.[18–21]

In contrast to active TB, the impact of prior pulmonary TB (PTB) in the treatment outcomes of critically ill patients with ICU admission has been much less frequently evaluated. Considering the pulmonary sequelae of TB,[22] identifying the impact of prior PTB in ICU-admitted pneumonia patients would be of clinical importance. Investigating the role of prior PTB in treatment outcomes of HCAP and CAP patients will also help us explore the clinical difference between HCAP and CAP. The aim of the present study was to evaluate the impact of prior PTB on treatment outcomes among HCAP and CAP patients requiring ICU admission. The occurrence of organ failure and the presence of microbiological pathogens were also assessed.

Methods

Patients

This nationwide, multi-center, retrospective study included six referral medical centers in Taiwan. The details of the study design have been previously described.[9] Briefly, hospitalized patients diagnosed with CAP and HCAP from January 2007 to December 2007 were eligible for enrollment, but only patients with documented ICU admission were included for analysis. The diagnosis of pneumonia was based on novel, abnormal chest radiographic findings with the growth of microorganisms in cultures of respiratory specimens, or with documented improvement after antibiotics treatment. The exclusion criteria were as follows: (1) patients younger than 20 years of age, (2) no ICU admission, (3) documented lung cancer with obstructive pneumonitis, (4) concomitant active TB, or (5) inadequate data for review. The Institutional Review Board of the six participating medical centers approved the study, and the need for informed consent was waived.

Definition of CAP and HCAP

HCAP and CAP were defined as in previous report.[23,24] Patients presenting with pneumonia diagnosed within 48 h after hospitalization were identified as HCAP if one of the

following criteria was satisfied: (1) receiving radiation therapy or chemotherapy at an outpatient clinic; (2) receiving regular dialysis at an outpatient clinic; (3) residing in a nursing home; or (4) undergoing repeated hospitalization within 90 days prior to the episode of current pneumonia. Pneumonia patients diagnosed within 48 h after hospitalization were included as CAP if none of the HCAP criteria were met.

Identification of prior PTB

A history of prior PTB was determined by a complete treatment record from the registration database of the Centers for Disease Control (CDC) in Taiwan and the medical records from each participating hospital. In Taiwan, enforcements are in place to ensure that all the cases of active TB are registered in the database of the CDC within 7 days of diagnosis. The information of anti-TB treatment outcome was also recorded in the database.

Clinical evaluation

The demographic profiles and clinical characteristics of the cases were acquired from the medical records. The severities of pneumonia were assessed using the pneumonia severity index (PSI).[25] The microorganisms in respiratory specimens were recorded and categorized as gram-positive coccus and/or gram-negative bacilli. In particular, the presence of ESKAPE (Enterococcus faecium, *Staphylococcus aureus*, *Klebsiella pneumoniae*, *Acinetobacter baumannii*, *Pseudomonas aeruginosa*, and Enterobacter species) pathogens in respiratory specimens obtained during the hospital stay was analyzed.[26]

Outcomes measurement

The use of empirical antibiotics were guided by the treatment guidelines of CAP and HCAP,[23,24] and adjusted according to the results of culture when available. The treatment outcomes of the ICU-admitted patients with pneumonia evaluated in the present study included 30-day mortality, length of ICU stay, length of hospital stay, and rate of long-term ventilator dependence. The occurrence of organ dysfunction, including respiratory failure, septic shock, altered mental status, renal dysfunction, liver dysfunction, coagulopathy, and thrombocytopenia, was also analyzed.

Statistically analysis

Continuous variables between subgroups were compared using independent t tests or a Mann—Whitney U test. Categorical variables were compared using Pearson's chi-square or Fisher's exact tests. Binary logistic regression analysis with stepwise selection was performed to determine the independent variables associated with the mortality in patients with CAP and HCAP, and hazard ratios (HRs) with their 95% confidence intervals (CI) were presented. A p value < 0.1 in the univariate analysis was required for a variable to be entered into the multivariate model. The survival time was estimated by the Kaplan—Meier method and compared with the log-rank test. Statistical analysis was performed using SPSS software, version 20.0 (SPSS Inc., Chicago, IL, USA). A p value < 0.05 was considered statistically significant.

Results

Patient characteristics

A total of 1657 hospitalized patients with CAP and HCAP from six hospitals were enrolled in this study. Of these patients, 1183 were excluded due to no ICU admission, and an additional 60 were excluded due to lung cancer with obstructive pneumonitis, age below 20 years, or incomplete data. A flow diagram showing the number of cases and the reasons for exclusion is shown in Fig. 1. Finally, 414 patients with ICU admission, including 176 CAP cases and 238 HCAP cases, were included for analysis. Among these patients, 301 (72.7%) were male, 166 (40.1%) had a smoking habit, 150 (36.2%) had diabetes mellitus, 143 (34.5%) had cardiovascular diseases, and 81 (19.6%) had malignant diseases. The mean age was 71.2 $\pm$ 14.0 years. The proportions of prior PTB were 10.2% (18/176) in patients with CAP and 7.1% (17/238) in patients with HCAP. The demographic characteristics of patients with CAP and HCAP included in the study are summarized in Table 1. When compared with CAP cases without prior PTB, patients with CAP and prior PTB were more likely to have diabetes mellitus ($p = 0.021$). Otherwise, there were no significant differences in age, sex, and other comorbidities between CAP patients with and without prior PTB. In patients with HCAP, the demographic characteristics were comparable between cases with and without prior PTB (Table 1). The diagnostic date of prior PTB were available in 16 CAP and 16 HAP cases. The mean duration from prior PTB to current pneumonia episode were 6.86 $\pm$ 6.0 years in CAP patients and 4.16 $\pm$ 4.11 years. There were no statistically significant differences between the two groups.

Clinical and microbiological presentations

The clinical and microbiological presentations of ICU-admitted patients with CAP and HCAP are summarized in Table 2. The mean PSI score was 133.2 $\pm$ 35.1 in CAP patients and 148.0 $\pm$ 37.9 in HCAP patients. In both CAP and HCAP cases, no difference in PSI scores between patients with and without prior PTB was observed. Among the included patients, respiratory failure was the most common organ dysfunction, followed by septic shock, within 48 h of admission. There was no difference in the proportion of various organ dysfunctions between patients with and without prior PTB in both CAP and HCAP cases. The microbiological characteristics are shown in Table 2. The proportions of gram-positive and gram-negative pathogens in sputum were similar in both CAP and HCAP patients with or without prior PTB. The presence of ESKAPE pathogens in respiratory specimens was noted in 44.3% patients with CAP and 39.5% patients with HCAP. Of these, *K. pneumoniae* was the most common ESKAPE pathogen followed by *P. aeruginosa*. As shown in Table 2, the distribution of ESKAPE pathogens was comparable between cases with and without prior PTB in both CAP and HCAP cases. However, a trend of lower ESKAPE pathogen load was noted in patients with

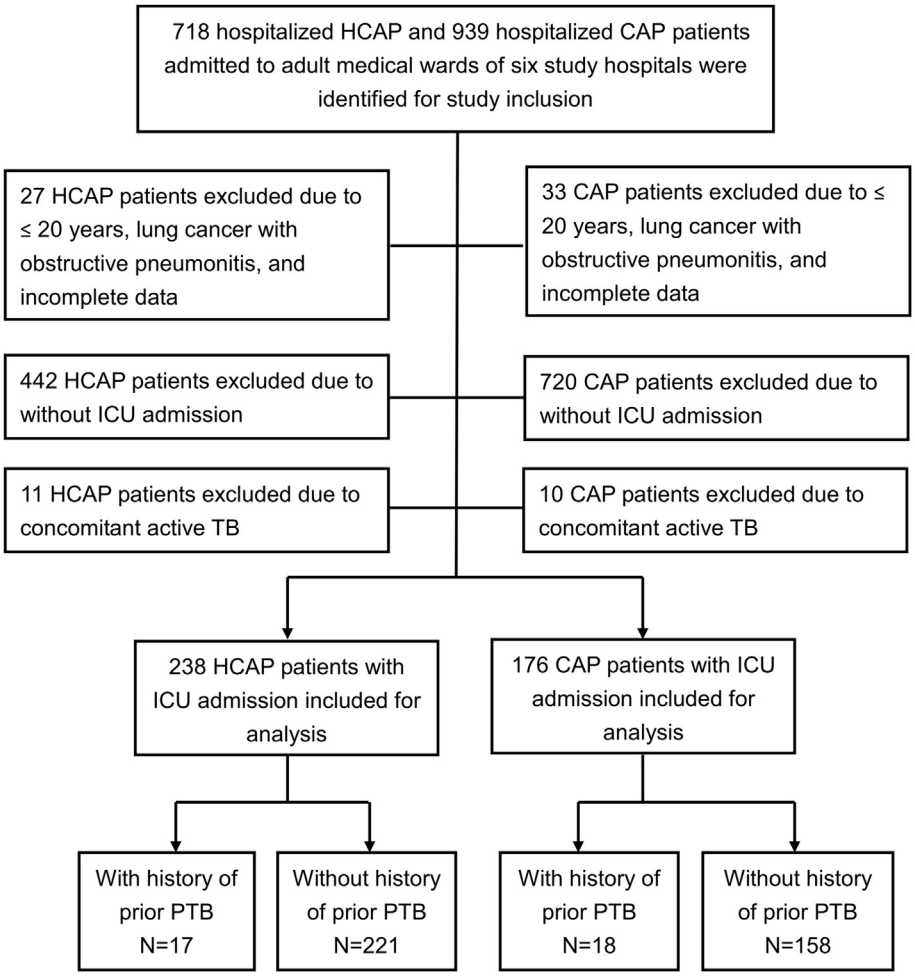

Fig. 1. Flow diagram demonstrating the number of cases and reasons for exclusion in this study. TB, tuberculosis; CAP, community-acquired pneumonia; HCAP, healthcare-associated pneumonia; ICU, intensive care unit.

HCAP and prior PTB (17.6% vs. 41.2%, p = 0.071) when compared to HCAP patients without prior PTB.

Treatment outcomes

The treatment outcomes of ICU-admitted patients with CAP and HCAP are summarized in Table 3. Overall, there was no difference in the length of ICU stay, length of hospital stay, ventilator dependence rate, or mortality rate between ICU-admitted pneumonia patients with and without prior PTB. In ICU-admitted CAP patients, cases with prior PTB had a higher 30-day mortality rate (38.9% vs. 16.5%, p = 0.021) compared with those without prior PTB. On the contrary, all the treatment outcomes were comparable between ICU-admitted HCAP patients with and without prior PTB, although a trend of lower mortality rates was noted in those with prior PTB (30-day mortality: 11.8% vs. 29.9%, p = 0.16; in-hospital mortality: 29.4% vs. 43.9%, p = 0.25).

Kaplan–Meier analysis of survival status according to a history of prior PTB is shown in Fig. 2. ICU-admitted patients with CAP and prior PTB had significantly higher mortality rates (log rank p = 0.021) compared to those without prior PTB (Fig. 2A). The curves separated early after admission. As shown in Fig. 2B, there was no statistical difference in mortality rate between ICU-admitted HCAP patients with and without prior PTB (log rank p = 0.127), although a trend of lower mortality rates was noted in those with prior PTB.

Clinical factors associated with 30-days mortality

Univariate and multivariate Cox regression analyses were performed to identify clinical factors associated with 30-day mortality in ICU-admitted patients with CAP and HCAP. As shown in Table 4, in ICU-admitted CAP patients, the clinical factors that significantly associated with 30-day mortality in univariate analysis included history of prior PTB, higher PSI scores, and diabetes mellitus. In the multivariate analysis, independent factors associated with higher 30-day mortality rate were prior PTB [hazard ratio (HR) 4.45, 95% CI 1.81–10.98, p = 0.001], higher PSI scores (HR 1.01, 95% CI 1.00–1.02, p = 0.046), diabetes mellitus (HR 4.10, 95% CI 1.62–10.36, p = 0.003), and autoimmune diseases (HR 5.16, 95% CI 1.19–22.33, p = 0.028). In ICU-admitted HCAP patients, clinical factors significantly associated with 30-day mortality in univariate analysis included smoking habit, higher PSI scores, malignant diseases, and chronic lung diseases. In the multivariate analysis,

Table 1 Demographic characteristics of ICU admitted CAP and HCAP patients with and without old TB[a].

	Overall patients, N = 414		P value	CAP patients, N = 176		P value	HCAP patients, N = 238		P value
	With prior TB, N = 35	Without prior TB, N = 379		With prior TB, N = 18	Without prior TB, N = 158		With prior TB, N = 17	Without prior TB, N = 221	
Mean age (SD)	74.7 (11.5)	70.9 (14.2)	0.12	71.8 (12.0)	71.1 (14.7)	0.84	77.9 (10.4)	70.8 (13.9)	0.058
Male gender	28 (80%)	273 (72%)	0.31	15 (83.3%)	118 (74.7%)	0.57	13 (76.5%)	155 (70.1%)	0.58
Smoking habit	13 (37.1%)	153 (40.4%)	0.71	8 (44.4%)	69 (43.7%)	0.95	5 (29.4%)	84 (38.0%)	0.48
Comorbidities									
Malignancy	4 (11.4%)	77 (20.3%)	0.20	1 (5.6%)	15 (9.5%)	1.00	3 (17.6%)	62 (28.1%)	0.57
Chronic kidney disease	4 (11.4%)	54 (14.2%)	0.80	1 (5.6%)	13 (8.2%)	1.00	3 (17.6%)	41 (18.6%)	1.00
Chronic liver disease	3 (8.6%)	23 (6.1%)	0.47	2 (11.1%)	6 (3.8%)	0.19	1 (5.9%)	17 (7.7%)	1.00
Diabetes	16 (45.7%)	134 (35.4%)	0.22	11 (61.1%)	53 (33.5%)	0.021	5 (29.4%)	81 (36.7%)	0.55
Autoimmune disease	0	16 (4.2%)	0.38	0	4 (2.5%)	1.00	0 (0)	12 (5.4%)	1.00
Chronic lung disorders	28 (80%)	190 (50.1%)	0.001	15 (83.3%)	88 (55.7%)	0.024	13 (76.5%)	102 (46.2%)	0.016
Cardiovascular disease	13 (37.1%)	130 (34.3%)	0.74	7 (38.9%)	50 (31.6%)	0.53	6 (35.3%)	80 (36.2%)	1.00
Neurological disorder	9 (25.7%)	138 (36.4%)	0.21	2 (11.1%)	47 (29.7%)	0.10	7 (41.2%)	91 (41.2%)	1.00
Type of pneumonia			0.27						
CAP	18 (51.4%)	158 (41.7%)							
HCAP	17 (48.6%)	221 (58.3%)							

[a] The data are presented as n (%) unless otherwise stated.

ICU, intensive care unit; CAP, community acquired pneumonia; HCAP, healthcare-associated pneumonia; TB, tuberculosis; SD, standard deviation.

independent factors associated with higher 30-day mortality rates were smoking habit (HR 1.69, 95% CI 1.02−2.79, p = 0.041), higher PSI scores (HR 1.02, 95% CI 1.01−1.02, p = 0.001), and malignant diseases (HR 1.87, 95% CI 1.05−3.32, p = 0.033).

Discussion

It is widely reported that ICU-admitted patients with CAP and active TB had worse outcomes, compared to those without active TB, although the empirical use of fluoroquinolones may improve their survival.[14,27] Hospitalized patients with HCAP and active TB also had more organ dysfunction, more ICU admission, and a longer length of hospital stay.[9] However, reports which evaluated the impact of prior PTB on treatment outcomes of pneumonia patients with ICU admission are scarce. In this study, although showing similar pneumonia severities and microbiological characteristics, ICU-admitted CAP patients with prior PTB had a significantly higher mortality rate than that without prior PTB. More importantly, we found that history of prior PTB was an independent factor associated with increased mortality in ICU-admitted patients with CAP, but not in ICU-admitted patients with HCAP. Our findings suggested a specific role of prior PTB in the treatment outcomes of the patients with CAP. It also highlighted the clinical differences between CAP and HCAP patients that require ICU admission.

The negative impact of prior PTB in treatment outcomes of pneumonia patients could be multifactorial. Prior PTB had been reported to increase the risk of several pulmonary disorders, such as lung cancer, chronic obstructive pulmonary disease, and bronchiectasis.[28,29] Elevated or unchanged serum concentration of interleukin-6 and interleukin-10, were noted in some patients who completed the anti-TB therapy, which suggested that systemic inflammation may persist beyond the completion of TB treatment.[30] The persistent inflammatory responses may lead to an increased risk of systemic disorders,[31−33] which may in turn worsen the prognosis of patients with pneumonia. Similarly, pulmonary disorders related to prior PTB such as structural lung disorders and bronchiectasis may also cause dysregulation of local immunity, which may increase the risk of bacterial infection and further compromise the treatment outcome in patients with pneumonia.[34]

Interestingly, we found that the negative impact of prior PTB in treatment outcome is only found in CAP patients, not in HCAP patients. Considering the high proportions of comorbidities and high PSI scores in HCAP patients, we speculated that the negative impact of prior PTB on treatment outcome may be masked by the other comorbidities. Our multivariate analysis also demonstrated that the independent factors associated with mortality in HCAP patients included malignant and autoimmune diseases, but not prior PTB. On the contrary, the proportions of comorbidities are fewer in CAP patients, and the impact of CAP

Table 2 Clinical and microbiological presentations of ICU admitted CAP and HCAP patients with and without old TB[a].

	CAP patients, N = 176		P value	HCAP patients, N = 238		P value
	With old TB, N = 18	Without old TB, N = 158		With old TB, N = 17	Without old TB, N = 221	
PSI score (SD)	139.6 (41.6)	132.4 (32.3)	0.45	148.5 (41.1)	148.0 (37.8)	0.75
CURB65 score (SD)	2.8 (1.2)	2.2 (1.2)	0.034	2.0 (0.9)	2.3 (1.2)	0.45
Bilateral lung involvement	11 (61.1%)	96 (60.8%)	0.98	11 (64.7%)	132 (59.7%)	0.68
Multi-lobar involvement	11 (61.1%)	114 (72.2%)	0.33	14 (82.4%)	158 (71.5%)	0.41
Organ dysfunction within 48 h						
Respiratory failure	15 (83.3%)	105 (66.5%)	0.15	10 (58.8%)	165 (74.7%)	0.15
Septic shock	6 (33.3%)	42 (26.6%)	0.58	3 (17.6%)	76 (34.4%)	0.16
Altered mental status	7 (38.9%)	31 (19.6%)	0.07	4 (23.5%)	80 (36.2%)	0.29
Acute kidney injury	1 (5.6%)	17 (10.8%)	0.49	5 (29.4%)	49 (22.2%)	0.49
Liver dysfunction	0	0	—	0	1 (0.5%)	1.00
Coagulopathy	0	5 (3.2%)	1.00	1 (5.9%)	10 (4.5%)	0.56
Thrombocytopenia	0	14 (8.9%)	0.37	0	28 (12.7%)	0.23
Numbers of organ failure (SD)	1.56 (1.10)	1.35 (1.15)	0.39	1.08 (1.06)	0.98 (1.22)	0.15
Pathogen in sputum culture						
Gram positive	3 (16.7%)	27 (17.1%)	0.96	1 (5.9%)	28 (12.7%)	0.70
Gram negative	10 (55.6%)	76 (48.1%)	0.55	4 (23.5%)	85 (38.5%)	0.22
ESKAPE pathogens						
Yes	8 (44.4%)	70 (44.3%)	0.99	3 (17.6%)	91 (41.2%)	0.071
No	10 (55.6%)	88 (55.7%)		14 (82.4%)	130 (58.8%)	
E. faecium	0	3 (1.9%)		0	1 (0.5%)	
S. aureus	1 (5.6%)	14 (8.9%)		0	19 (8.6%)	
K. pneumoniae	3 (16.7%)	27 (17.1%)		1 (5.9%)	32 (14.5%)	
A. baumannii	2 (11.1%)	7 (4.4%)		1 (5.9%)	11 (5%)	
P. aeruginosa	2 (11.1%)	21 (13.3%)		1 (5.9%)	37 (16.7%)	
Enterobacter spp	2 (11.1%)	17 (10.8%)		1 (5.9%)	26 (11.8%)	

[a] The data are presented as n (%) unless otherwise stated.
ICU, intensive care unit; CAP, community acquired pneumonia; HCAP, healthcare-associated pneumonia; TB, tuberculosis; SD, standard deviation; PSI, pneumonia severity index; CURB65, confusion, urea, respiratory rate, blood pressure, age 65; ESKAPE, *Enterococcus faecium*, *Staphylococcus aureus*, *Klebsiella pneumoniae*, *Acinetobacter baumannii*, *Pseudomonas aeruginosa and Enterobacter* spp.

can be easily highlighted. Our findings suggest that a history of prior PTB plays a specific role in the treatment responses of CAP patients requiring ICU admission. History and radiologic evidences that are suggestive of prior PTB should be carefully reviewed in CAP patients that require ICU admission, and these patients should be aggressively treated to improve their treatment outcomes.

It remains controversial whether HCAP is a specific clinical entity, and HCAP is removed from the concept of HAP/VAP in the current guidelines as many studies revealed

Table 3 Disease severities and treatment outcomes of ICU admitted CAP and HCAP patients with and without old TB[a].

	CAP patients, N = 176		P value	HCAP patients, N = 238		P value
	With old TB, N = 18	Without old TB, N = 158		With old TB, N = 17	Without old TB, N = 221	
Length of ICU stay (SD)						
All patients	23.1 (29.7)	19.2 (21.6)	0.89	21.8 (22.0)	16.5 (14.4)	0.45
Survivors	28.5 (32.1)	19.3 (21.7)	0.39	15.5 (12.0)	16.8 (14.0)	0.84
Non-survivors	16.3 (26.9)	19.1 (21.7)	0.54	37.0 (33.6)	16.0 (14.9)	0.13
Length of hospital stay (SD)						
All patients	33.6 (32.7)	34.8 (27.6)	0.40	42.7 (32.9)	32.5 (28.1)	0.17
Survivors	44.5 (34.2)	36.3 (26.9)	0.60	42.8 (34.5)	37.3 (31.4)	0.62
Non-survivors	20.0 (26.8)	31.7 (29.0)	0.25	42.2 (32.8)	26.2 (21.7)	0.22
Mortality						
30-day mortality	7 (38.9%)	26 (16.5%)	0.021	2 (11.8%)	66 (29.9%)	0.16
In-hospital mortality	8 (44.4%)	51 (32.3%)	0.30	5 (29.4%)	97 (43.9%)	0.25

[a] The data are presented as n (%) unless otherwise stated.
ICU, intensive care unit; CAP, community acquired pneumonia; HCAP, healthcare-associated pneumonia; TB, tuberculosis; SD, standard deviation.

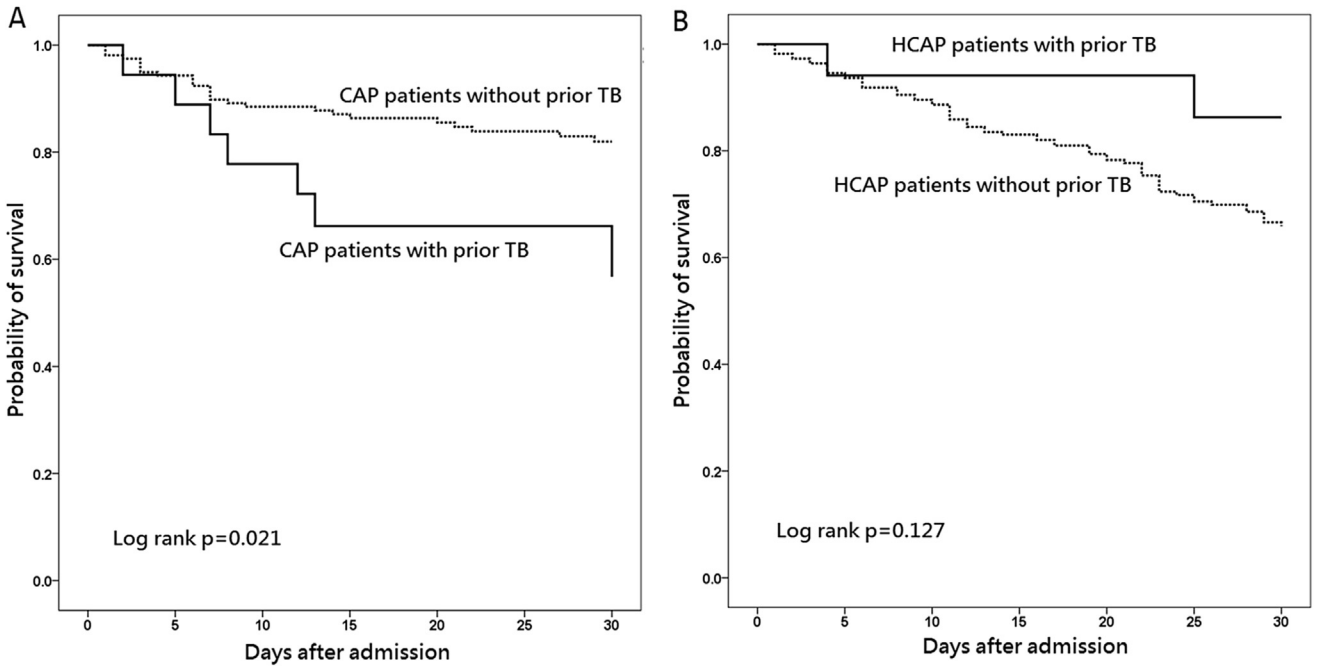

Fig. 2. Kaplan–Meier survival curves of ICU-admitted pneumonia cases with and without history of prior TB. A) CAP patients. B) HCAP patients. TB, tuberculosis; CAP, community-acquired pneumonia; HCAP, healthcare-associated pneumonia; ICU, intensive care unit.

that patients defined as HCAP are not at high risk for multidrug resistant pathogens.[3,35–37] On the contrary, it is recommended that HCAP is included in the upcoming CAP guidelines because HCAP patients frequently present from the community and are initially cared for in the emergency department.[3] However, the clinical differences between

Table 4 Univariate and multivariate analysis of demographic factors associated with 30-day mortality in CAP and HAP patients with ICU admission[a].

	CAP patients				HCAP patients			
	Univariate		Multivariate		Univariate		Multivariate	
	HR (95% CI)	P value	HR (95% CI)	P value	HR (95% CI)	P value	HR (95% CI)	P value
Age	1.00 (0.98–1.02)	0.99			0.99 (0.98–1.01)	0.44		
Male gender	0.97 (0.44–2.14)	0.93			0.77 (0.44–1.33)	0.34		
Smoking habit	0.65 (0.32–1.35)	0.25			2.10 (1.30–3.38)	0.002		
History of prior TB	2.57 (1.12–5.93)	0.027	3.86 (1.54–9.71)	0.004	0.35 (0.09–1.44)	0.15		
CURB65 scores	1.51 (1.13–2.02)	0.005	1.40 (1.05–1.87)	0.024	1.50 (1.21–1.86)	<0.001	1.48 (1.18–1.84)	<0.001
Malignancy	2.32 (0.96–5.61)	0.06	3.03 (1.22–7.50)	0.017	3.42 (2.12–5.50)	<0.001	3.30 (2.04–5.33)	<0.001
Chronic kidney disease	0.68 (0.16–2.82)	0.59			1.08 (0.58–2.01)	0.82		
Chronic liver disease	0.63 (0.09–4.62)	0.65			1.73 (0.83–3.62)	0.15		
Diabetes	2.84 (1.17–6.87)	0.021	4.13 (1.63–10.47)	0.005	1.06 (0.65–1.73)	0.82		
Chronic lung disease	1.01 (0.50–2.04)	0.97			1.72 (1.06–2.80)	0.028		
Autoimmune disease	3.37 (0.81–14.10)	0.09	5.99 (1.36–26.38)	0.018	2.16 (0.93–5.00)	0.07	2.89 (1.24–6.74)	0.014
Cardiovascular disease	0.82 (0.38–1.77)	0.61			0.96 (0.58–1.59)	0.88		
Neurological disorder	0.52 (0.21–1.25)	0.14			0.61 (0.36–1.02)	0.06		

[a] Univariate and multivariate HR are derived from logistic regression analysis with stepwise selection procedure.
CAP, community acquired pneumonia; HCAP, healthcare-associated pneumonia; ICU, intensive care unit; TB, tuberculosis; HR, hazard ratio; CI, confidence interval; CURB65, confusion, urea, respiratory rate, blood pressure, age 65.

CAP and HCAP have been reported in previous reports and in the present study.[38] Furthermore, we identified different impacts of prior PTB on mortality between CAP and HCAP patients. Our findings suggested that HCAP is a specific entity with its unique clinical characteristics. More evidence is still required to conclude if HCAP and CAP belong to the same clinical entity.

This study has several limitations that are worth noting. Some relevant clinical parameters, such as the time delay in pneumonia diagnosis and the radiographic characteristics of prior PTB sequelae, were not obtained in our initial study design. History of prior PTB was determined based on the records in Taiwan CDC database; therefore, this study lacked patients with history of undiagnosed and/or untreated TB. The number of patients with prior PTB was relatively small in both CAP and HCAP cases, which may underestimate the impact of prior PTB on treatment outcomes. Currently there is no well-verified scoring tool to assess the severities of HCAP. Therefore the PSI score used in the present study would not be able to clearly discriminate the severities of HCAP patients with and without PTB. Finally, this study was carried out in a TB-endemic area with low human immunodeficiency virus (HIV) prevalence. Therefore, it is unlikely that these findings are applicable in areas with low TB incidence or high HIV prevalence.

In conclusion, this multi-center retrospective study demonstrated that among CAP patients requiring ICU admission, patients with prior PTB had higher 30-day mortality than those without prior PTB, and the history of prior PTB was an independent factor associated with mortality. The presence of prior PTB should be carefully pursued in the management of ICU-admitted CAP patients. Further studies are necessary to identify other clinical factors that may different impacts on treatment between CAP and HCAP cases.

Conflicts of interest

All authors declare no conflicts of interest.

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