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Original Article

Outcomes of corticosteroid treatment in critical Ill adult patients with respiratory viruses-related community acquired pneumonia — a propensity-matched case control study

Ching-Hao Hsu [a], Andrew Po-Liang Chen [b,c], Hsin-Pai Chen [a,b,*], Yu-Jiun Chan [d,e,f]

[a] *Division of Infectious Diseases, Department of Medicine, Taipei Veterans General Hospital, Taipei, Taiwan*
[b] *School of Medicine, National Yang Ming Chiao Tung University, Taipei, Taiwan*
[c] *Department of Critical Care Medicine, Taipei Veterans General Hospital, Taipei, Taiwan*
[d] *Division of Microbiology, Department of Pathology and Laboratory Medicine, Taipei Veterans General Hospital, Taipei, Taiwan*
[e] *Institute of Public Health, School of Medicine, National Yang Ming Chiao Tung University, Taipei, Taiwan*
[f] *Department of Infection Control, Taipei Veterans General Hospital, Taipei, Taiwan*

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KEYWORDS
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Abstract *Objectives:* To assess the outcomes of corticosteroid treatment in critically ill patients with respiratory virus–related community-acquired pneumonia (CAP).
Materials/methods: Adult patients who were admitted to the intensive care unit and had a polymerase chain reaction–confirmed diagnosis of respiratory virus–related CAP were included. Patients with and without corticosteroid treatment during the hospital course were retrospectively compared using a propensity score–matched case–control analysis.
Results: From January 2018 to December 2020, 194 adult patients were enrolled with 1:1 matching. The 14-day and 28-day mortality rates did not differ significantly between patients treated with and without corticosteroids (14-day mortality: 7% versus 14%, $P = 0.11$; 28-day

Abbreviations: CAP, community-acquired pneumonia; RV, respiratory virus; PCR, polymerase chain reaction; SARS-CoV, severe acute respiratory syndrome coronvirus; COVID-19, coronavirus disease 2019; RECOVERY, Randomised Evaluation of COVID-19 Therapy; ICU, intensive care unit; APACHE II, Acute Physiology and Chronic Health Evaluation II; ARDS, acute respiratory distress syndrome; CRP, c-reactive protein; CIs, confidence intervals; COPD, chronic obstructive pulmonary disease; OR, odds ratio; IQR, interquartile range.

* Corresponding author. Taipei Veterans General Hospital, 201 Shih-Pai Road, Sec. 2, Taipei 11247, Taiwan. Fax: +886 2 2873 5656.
E-mail address: chenhp1970tw@gmail.com (H.-P. Chen).

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mortality: 15% versus 20%, $P = 0.35$). However, multivariate analysis by using a Cox regression model revealed that corticosteroid treatment was an independent factor predicting decreased mortality (adjusted odds ratio, 0.46; 95% confidence interval, 0.22—0.97, $P = 0.04$). Subgroup analysis revealed lower 14-day and 28-day mortality rates in patients younger than 70 years treated with corticosteroids than in those not treated with corticosteroids (14-day mortality: 6% versus 23%; $P = 0.01$ and 28-day mortality: 12% versus 27%; $P = 0.04$).
Conclusions: Non-elderly patients with severe respiratory virus—related CAP are more likely to benefit from corticosteroid treatment than elderly patients.

Introduction

Community-acquired pneumonia (CAP) remains the leading cause of mortality and morbidity, posing a great burden to public health worldwide.[1] Many microorganisms are associated with CAP; however, unlike bacteria, the role of respiratory viruses (RVs) in CAP has been assessed in immunocompromised adults and children. With the rapid development of positive multiplex polymerase chain reaction (PCR), the role of RVs as causative agents of CAP in adults has been increasingly recognized.[2] Influenza virus is the best-known RV that causes severe pneumonia. Infections caused by other non-influenza RVs have also been reported to result in severe illness in both immunosuppressed and immunocompetent patients.[3—7] The outbreaks of severe acute respiratory syndrome coronavirus (SARS-CoV) in 2003 and influenza A (H1N1) in 2009 and the recent coronavirus disease 2019 (COVID-19) pandemic have highlighted the undeniable role of RVs in patients with severe pneumonia.

The host immune response plays a crucial role in viral pneumonia progression and end-organ damage.[8—12] Corticosteroids can suppress cell-mediated immune responses and the secretion of inflammatory cytokines, and they have been used to modulate host immune responses in some infectious diseases. Recently, the Randomised Evaluation of COVID-19 Therapy (RECOVERY) trial confirmed the role of corticosteroids in SARS-CoV-2. It revealed that the use of dexamethasone could reduce 28-day mortality in SARS-CoV-2 patients on respiratory support.[13] However, studies evaluating the efficacy of corticosteroid therapy in patients with influenza pneumonia have reported conflicting results.[14,15] We previously demonstrated that patients with RV-related lower respiratory tract infections treated with corticosteroids had marginally lower 14-day and 28-day mortality rates.[16] As corticosteroids potentially decrease viral clearance and increase the chance of secondary infections,[17] their beneficial effects in suppressing overactive immune responses must be weighed against the accompanying detrimental effects. Moreover, whether other clinical variables affect the therapeutic effects of corticosteroids in patients with RV-related CAP remains to be clarified.

In the RECOVERY trial, the therapeutic effect of corticosteroids was less prominent in patients older than 70 years.[13] In another study, higher 30-day mortality rates were noted in critically ill elderly patients with COVID-19 who received steroids.[18] Except for influenza and COVID-19, few studies have assessed the therapeutic role of corticosteroids in RV-related CAP. Furthermore, whether an age-specific difference exists in the therapeutic effects between young and elderly patients remains unknown.

This study assessed the therapeutic effects of corticosteroids among patients with severe RV-related CAP. The patients enrolled in this study overlapped with those enrolled in our previous study.[16]

Methods

Study population and design

This case—control study was approved by the Institutional Review Board of Taipei Veterans General Hospital. All critically ill patients admitted to the intensive care unit (ICU) from January 2018 to December 2020 with a diagnosis of CAP were retrospectively screened. All eligible patients who aged at least 20 years, required mechanical ventilation support, and had confirmed RV infection by a commercial PCR kit (BioFire FilmArray Atypical Pneumonia Panel, USA or xTAG Respiratory Virus Panel, Canada) for CAP survey, were included in this study. Additional detail including respiratory pathogen that can be detected by PCR, sampling procedures, and definition of CAP, is provided in an online data supplement.

Definitions and baseline measures

Demographic, comorbidity, and laboratory data for each patient were collected at the time of ICU admission. Patients were considered to be treated with systemic corticosteroids when a dosage equivalent to at least 7.5 mg of prednisolone per day was administered during ICU stay. Clinical severity at ICU admission was recorded using the Acute Physiology and Chronic Health Evaluation (APACHE) II.[19] Treatment decisions, including the use of corticosteroids, were determined based on the managing clinical physician's judgment. Data regarding adverse clinical outcomes, including secondary infections that occurred 48 h after admission, septic shock, acute kidney injury, acute respiratory distress syndrome (ARDS) based on the Berlin definition,[20] and the need for extracorporeal membrane oxygenation insertion, were also collected in this study.

Outcome measures

All-cause mortality within 28 days after initial presentation was assessed to measure the primary outcomes. The clinical status of patients on days 14 and 28 was scored on a 7-point ordinal scale modified from the World Health Organization guidelines.[21] Other outcomes included all-cause mortality in 14 days, durations of mechanical ventilation, ICU stay, and hospital admission. Prespecified analyses of the primary outcomes were performed in the six subgroups defined by the characteristics at initial presentation, namely age (<70 years versus ≥70 years), sex, level of respiratory support, presence or absence of influenza virus, initial C-reactive protein (CRP) levels, and APACHE II scores, to predict 28-day mortality risk.

Statistical analysis

To account for possible bias from disease severity, the patients' age, sex, and APACHE II scores were included in the calculation of the propensity score. The corticosteroid and non-corticosteroid groups were then matched in a 1:1 ratio without replacement based on the propensity score. The nearest neighbor technique was used with a match tolerance of 0.02.

Categorical variables were compared using the chi-squared test or Fisher exact test, as appropriate, and continuous variables were compared using the Mann—Whitney U test or Student's *t* test. Estimates of rates and risk ratios are presented using 95% confidence intervals (CIs). A univariate Cox regression model was used initially for potential variables that impact mortality; variables which showed significant or nearly significant differences ($P < 0.08$) on univariate analysis were then entered multivariate analysis to derive the associations between mortality rate and the predictor variables. Cumulative mortality and successful cessation of invasive mechanical ventilation over the 28-day period were analyzed by the Kaplan—Meier method and compared by long-rank test. A *P* value < 0.05 was considered statistically significant.

Results

Patient characteristics

During the study period, a total of 12,571 patients underwent multiplex PCR assessments for detecting RVs, and 2524 (20%) of them were confirmed to have RV infections. Of these, 385 critically ill patients who were admitted to the ICU due to respiratory failure were included for further analyses (Fig. 1). In total, 182 patients were excluded: 40 patients who were repeatedly tested, 42 non-adult patients, 90 patients with confirmed hospital-acquired pneumonia at presentation, and 10 patients with incomplete chart records. After 1:1 propensity score matching, 194 patients were included for further analyses: 97 patients who received corticosteroids and 97 patients who did not.

The baseline characteristics of patients who received corticosteroids and those who did not are compared in Table 1. The ratio of underlying chronic obstructive pulmonary disease (COPD) and ARDS at initial presentation was higher in patients who received corticosteroids than in those who did not ($P < 0.001$ for both); however, no differences in demographic characteristics and underlying comorbidities were noted between the two groups. Moreover, clinical and biochemical parameters, including oxygen demand, disease severity scores, and levels of inflammation markers (such as white blood cell counts and CRP levels), did not differ between the patient groups.

Distribution of RVs

The multiplex PCR panel identified a total of 212 pathogens in 194 patients. Most of the PCR testing was performed immediately (median [interquartile range, IQR] = 1 [1—3] day between ICU admission and PCR testing) after admission to ICU. Of these, 166 (86%) patients had single virus infections and 28 (14%) had multiple virus infections (27 had coinfections with two viruses and one had coinfections with three viruses). The most commonly identified RV was rhinovirus/enterovirus (n = 73; 34%), followed by influenza virus (n = 54; 26%) and parainfluenza virus (n = 29; 14%) (Fig. S1). Among the 28 patients with multiple virus infections, 16 (57%) had infections caused by influenza virus along with other RVs.

Corticosteroid and antimicrobial treatments

In 194 enrolled patients, 48 of 97 (50%) patients in corticosteroid group and 47 of 97 (49%) in non-corticosteroid had concurrent infection; most of the concurrent pathogen were bacteria (n = 76 of 95; 80%). All patients received antibacterial agents during the disease course. All patients with influenza virus infections (n = 54 of 194; 28%) received antiviral treatment with oseltamivir or peramivir.

In 97 patients who received corticosteroids, most patients received corticosteroids immediately after ICU admission (median [IQR] = 0 [0—0] day between ICU admission and corticosteroid treatment). The median (IQR) duration of corticosteroid therapy was 15 (8—26) days and the median (IQR) daily dose equivalent to prednisolone administered in the ICU was 52 (22—79) mg. In 32 (33%) and 25 (26%) patients, corticosteroids were used for ARDS and acute exacerbation of COPD, respectively. Other reasons for corticosteroid use included septic shock, interstitial lung disease, and pneumonitis caused by miscellaneous reasons (Table 2).

Outcomes in overall patients

The 14-day and 28-day mortality rates did not differ significantly between the corticosteroid and non-corticosteroid groups at the initial analysis (14-day mortality: 7% versus 14%, $P = 0.11$; 28-day mortality: 15% versus 20%, $P = 0.33$; Fig. 2A & B). However, multivariate survival analysis using a Cox regression model revealed that corticosteroid treatment was an independent factor associated with decreased mortality (adjusted odds ratio [OR], 0.46; 95% CI, 0.22—0.97; $P = 0.04$; Table 3). In all patients, the median (IQR) duration from symptom onset to presentation was 2 (1—4) days and the median (IQR) duration from presentation to ICU admission was 0 (0—1) days. The

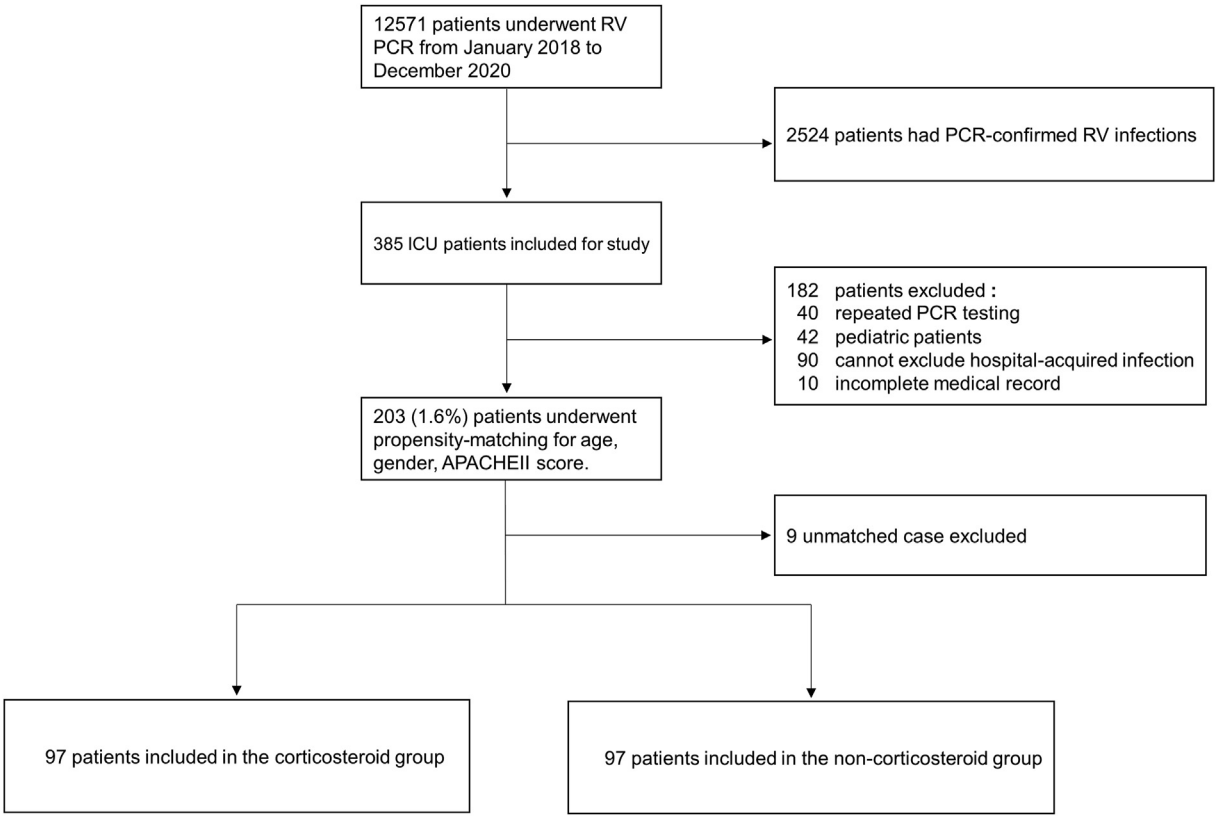

Figure 1. Flowchart of study enrollment, exclusion, and allocation.

durations of invasive mechanical ventilation and ICU stay were longer in the corticosteroid group than in the non-corticosteroid group ($P < 0.001$ for both; Table 2). The ventilator-free rates within 14 days and 28 days were lower in the corticosteroid group than in the non-corticosteroid group (14 days: 30% versus 47%, $P = 0.05$; 28 days: 49% versus 63%, $P = 0.05$; Fig. S2, Panel A & B). The incidence of secondary infections during the ICU course was higher in patients treated with corticosteroids (75% versus 58%; $P = 0.01$), with *Acinetobacter baumannii* being the most common pathogen (n = 37 of 210, 18%), followed by *Burkholderia cepacia* (n = 26 of 210, 12%) and *Klebsiella pneumoniae* (n = 20 of 210, 9%). Other clinical outcome measures did not differ between the two groups.

Survival associated with corticosteroid treatment in patients younger than 70 years

We further analyzed whether younger patients were more likely to benefit from corticosteroid treatment. In total, 100 patients younger than 70 years were included in this study. Table S1 compares the baseline clinical characteristics between the 52 (52%) patients who received corticosteroids and 48 (48%) patients who did not. A similar distribution of demographic characteristics and underlying diseases was observed, with a higher ratio of COPD being observed in the corticosteroid group ($P < 0.001$). The Kaplan—Meier survival curves of 14-day and 28-day mortality rates demonstrated lower mortality rates in the corticosteroid group than in the non-corticosteroid group. In particular, the 14-day mortality rates were 6% (3/52) in the corticosteroid group and 23% (11/48) in the non-corticosteroid group ($P = 0.01$ by log-rank test; Fig. 2E), and the 28-day mortality rates were 12% (6/52) in the corticosteroid group and 27% (13/48) in the non-corticosteroid group ($P = 0.04$; Fig. 2F). Multivariate Cox regression analysis revealed that in patients younger than 70 years, the use of corticosteroids during the disease course was significantly associated with a decreased 28-day mortality rate (adjusted OR, 0.17; 95% CI, 0.06—0.48; $P < 0.001$; Table S2). The durations of invasive mechanical ventilation and ICU stay were longer in patients who received corticosteroids than in those who did not ($P < 0.001$ for both; Table S3). The ratio of successful cessation of invasive mechanical ventilation within 14 days and 28 days did not differ between the two groups (Fig. S2, Panel C & D).

Corticosteroid treatment and survival associated with the presence or absence of influenza virus

The detection of influenza virus was not associated with a higher 28-day in-hospital mortality rate in the Cox regression model (Table 3). In a prespecified subgroup analysis based on the detection of influenza virus in the respiratory specimens, the 14-day and 28-day mortality rates did not differ between patients who received corticosteroids and those who did not in both influenza and non-influenza groups (Fig. S3). We then analyzed whether young patients with influenza virus infections would possibly benefit

Table 1 Baseline demographic, clinical, and laboratory characteristics of critically ill patients with respiratory virus-related community-acquired pneumonia: overall patients.

Characteristic	Corticosteroid treatment (n = 97)	Non-corticosteroid treatment (n = 97)	*P* value
Male sex	61 (63)	58 (60)	0.66
Age, years (mean ± SD)	70.6 ± 15.0	70.4 ± 17.8	0.94
Body mass index (mean ± SD)	22.6 ± 5.2	23.5 ± 4.9	0.21
Sample collected from lower respiratory tract	32 (33)	22 (23)	0.15
Underlying disease			
Chronic heart failure	13 (13)	17 (18)	0.43
Chronic renal disease	15 (16)	24 (25)	0.11
Chronic obstructive pulmonary disease	34 (35)	10 (10)	<0.001
Diabetes mellitus	26 (27)	29 (30)	0.63
Hypertension	40 (41)	44 (45)	0.56
Solid tumor	24 (25)	24 (25)	1.00
Hematologic malignancy	4 (4)	5 (5)	0.73
Solid organ transplantation	3 (3)	2 (2)	0.65
Signs at ICU admission			
APACHE II score (mean ± SD)	20.0 ± 7.7	20.2 ± 7.6	0.87
SOFA score (mean ± SD)	7.2 ± 2.3	7.2 ± 2.4	0.93
Intubation with mechanical ventilation	69 (71)	71 (73)	0.75
Temperature, °C (mean ± SD)	37.2 ± 1.1	36.9 ± 1.4	0.08
Heart rate, beats/min (mean ± SD)	106.0 ± 21.4	98.0 ± 26.1	0.20
Mean blood pressure, mmHg (mean ± SD)	101.9 ± 23.8	100.5 ± 23.5	0.67
PaO2/FiO_2 ratio (mean ± SD)	209.0 ± 120.9	200.0 ± 116.2	0.52
WBC count, per 1000/μL (mean ± SD)	11.8 ± 7.6	12.1 ± 7.1	0.65
Platelet count, per 1000/μL (mean ± SD)	209.6 ± 93.9	190.1 ± 93.6	0.15
Creatinine, mg/dL (mean ± SD)	1.5 ± 1.4	1.9 ± 1.3	0.10
C-reactive protein, mg/dL (mean ± SD)	10.9 ± 10.6	10.1 ± 11.8	0.70
Sodium, mmol/L (mean ± SD)	138.4 ± 6.0	137.2 ± 6.2	0.31
Potassium, mmol/L (mean ± SD)	4.2 ± 0.8	4.3 ± 0.8	0.59

SD, standard deviation; ICU, intensive care unit; APACHE, Acute physiology and chronic health evaluation; SOFA, Sequential organ failure assessment; PaO2, partial pressure of oxygen in the arterial blood; FIO_2, fraction of inspired oxygen; WBC, white blood cell.
Data are presented as No. (%), unless otherwise specified.

from corticosteroid treatment. In the 100 patients younger than 70 years, the use of corticosteroids was associated with a trend of lower 14-day and 28-day mortality rates, but non-significantly (Fig. S4).

Discussion

Our findings revealed that the administration of corticosteroids was associated with decreased 28-day mortality rates among adult patients younger than 70 years who had severe RV-related CAP. However, corticosteroid treatment did not exhibit beneficial effects in patients aged 70 years and older, probably because of the adverse effects of steroids in the elderly population. The survival benefit was associated with an increased duration of ICU stay and an increased rate of secondary infections.

RVs can trigger an overwhelming immune response in the host, resulting in neutrophil and macrophage accumulation in the lungs and causing severe pulmonary damage.[22—24] Inhibition of inflammatory cytokines may mitigate respiratory distress and improve the survival of patients with critically ill diseases. Corticosteroids suppress inflammatory reactions by directly binding to the regulatory regions of pro-inflammatory genes and inhibiting the production of inflammatory cytokines.[25,26] Corticosteroids have been used to ameliorate the overwhelming inflammatory response in patients with viral pneumonia, including that caused by influenza virus, SARS-CoV, Middle East respiratory syndrome CoV, and SARS-CoV-2. However, except for the RECOVERY trial of COVID-19, controversial results have been reported regarding the use of corticosteroids, with few studies supporting the therapeutic role of corticosteroids against RV infections.

Age-related differences in the effects of corticosteroids may explain these controversial results. Compared with the elderly population, young adults have more mature and complete innate and adaptive immune responses, leading to a more appropriate immune response when dealing with infections.[27] In a study on severe influenza pneumonia, corticosteroid therapy was associated with reduced mortality rates in patients younger than 60 years; however, such beneficial effects were not observed in patients older than 60 years.[28] Our findings are in agreement with these findings. We found that in critically ill patients with RV-related-CAP who were aged less than 70 years, corticosteroid treatment was associated with reduced 14-day and 28-day mortality rates; however, patients aged 70 years and older did not benefit from corticosteroid treatment. These

Table 2 Clinical presentations and outcomes of critically ill patients with respiratory virus-related community-acquired pneumonia: overall patients.

Characteristic	Corticosteroid treatment (n = 97)	Non-corticosteroid treatment (n = 97)	*P* value
Corticosteroid use			
Interval between ICU admission and corticosteroid days: median (IQR)	0 (0—0)	NA	
Duration, days: median (IQR)	15 (8—26)	NA	
Dose equivalent (prednisolone), mg/day: median (IQR)	52 (22.0—78.6)	NA	
Methylprednisolone	75 (77)	NA	
For ARDS	32 (33)	NA	
For COPD	25 (26)	NA	
For other reason[a]	40 (41)	NA	
Adverse events in disease course			
Co-infection	48 (50)	47 (49)	0.89
Secondary infection	73 (75)	56 (58)	0.01
Acute kidney injury	49 (51)	57 (59)	0.25
New hemodialysis	12 (12)	15 (16)	0.53
ARDS	43 (44)	18 (19)	<0.001
ECMO use	8 (8)	6 (6)	0.58
Acute gastrointestinal bleeding	11 (11)	11 (11)	1.00
Shock	50 (52)	50 (52)	1.00
Clinical outcome			
14-day ordinal scale (mean ± SD)	4.9 ± 1.6	4.6 ± 1.8	0.30
28-day ordinal scale (mean ± SD)	4.1 ± 2.2	3.6 ± 2.3	0.20
Length of hospital stay, days (mean ± SD)	37.3 ± 32.0	30.2 ± 28.6	0.10
Length of ICU stay, days (mean ± SD)	21.3 ± 20.8	13.9 ± 13.3	<0.001
Length of invasive ventilation, days (mean ± SD)[b]	27.0 ± 27.6	13.6 ± 14.1	<0.001
Invasive ventilator-free within 14 days[b]	21 (30)	33 (47)	0.05
Invasive ventilator-free within 28 days[b]	34 (49)	45 (63)	0.09
Mortality rate			
14-day deaths	7 (7)	14 (14)	0.11
28-day deaths	15 (15)	20 (21)	0.35

[a] Other reasons for corticosteroid use included septic shock, interstitial lung disease, and pneumonitis caused by miscellaneous reasons.

[b] Patients without intubation were excluded. Case numbers for each group: corticosteroid, n = 69; non-corticosteroid, n = 71.

IQR, interquartile range; NA, not applicable; COPD, chronic obstructive pulmonary disease; ECMO, extracorporeal membrane oxygenation; SD, standard deviation; ARDS, acute respiratory distress syndrome; ICU, intensive care unit.

Data are presented as No. (%), unless otherwise specified.

findings are also in accordance with those of a recent study on COVID-19, which reported a correlation between steroid use and increased mortality in critically ill patients aged 70 years and older.[18] The mechanism underlying such age-specific discrepancies in the therapeutic effects of corticosteroids remains unclear but may be associated with their adverse effects. We hypothesized that corticosteroids enabled critically ill patients to survive the initial inflammatory stage of the disease and progress to a sustained illness phase with secondary infections. Therefore, patients

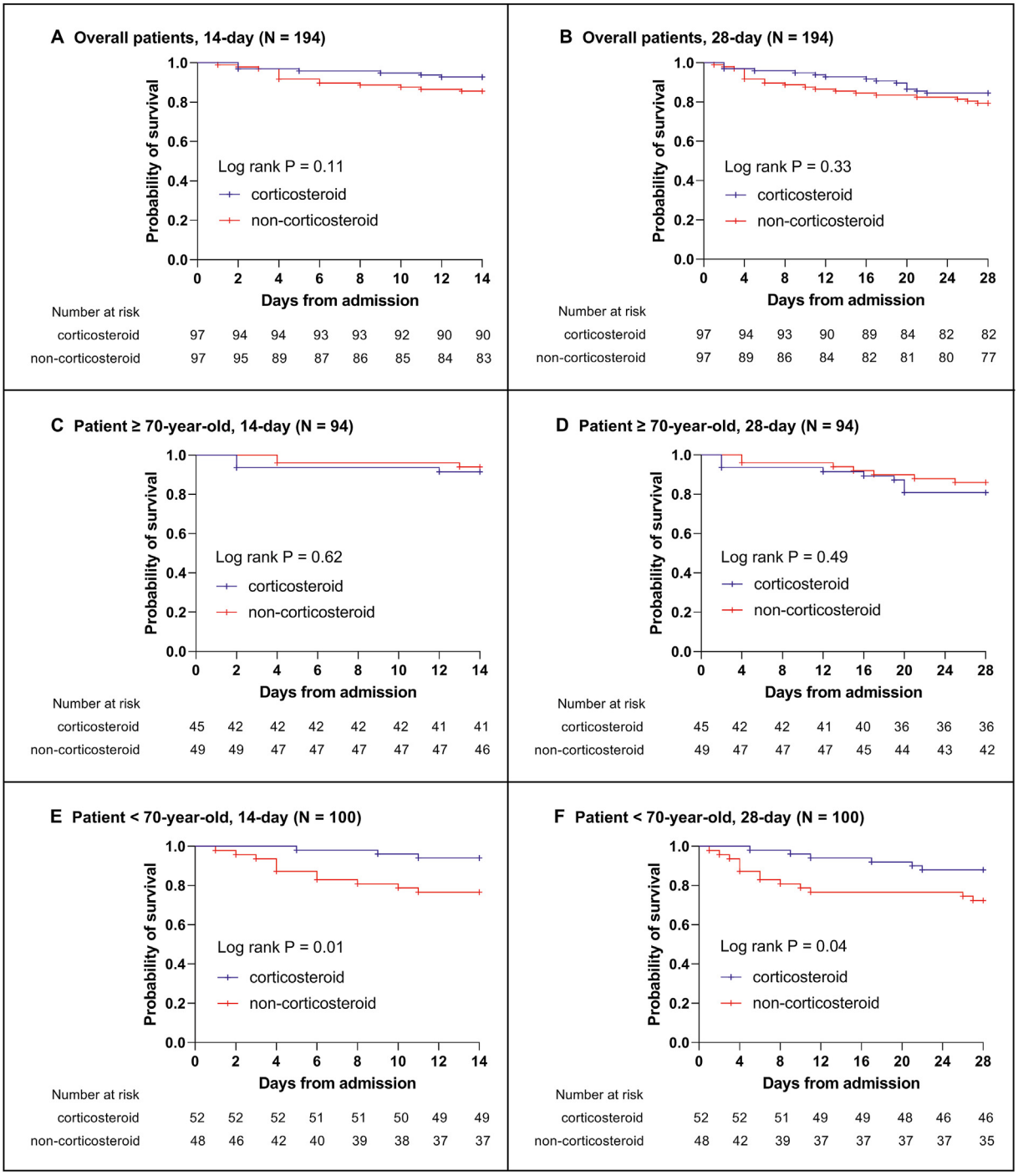

Figure 2. Kaplan—Meier curves of 14-day and 28-day survival rates among patients with respiratory virus-related community-acquired pneumonia. Patients who received corticosteroids (blue line) were compared with those who did not (red line). (I) Overall patients (Panels A and B). (II) Patients aged 70 years or older (Panels C and D). (III) Patients younger than 70 years (Panels E and F).

who received corticosteroids had longer durations of ICU stay and invasive mechanical ventilation and a higher incidence of secondary infections.

The timing of corticosteroid administration may also be crucial. Since corticosteroids delays viral clearance,[17] early use of corticosteroids in patients with mild RV infection may be harmful. On the other hand, the anti-inflammatory effect of corticosteroids potentially benefits severe viral pneumonia when the disease progresses to profound inflammation, as had been indicated in the RECOVERY trial of COVID-19.[13] In our study, patients were given corticosteroid treatment soon after ICU admission. Timely administration of corticosteroid when the disease turned into a hyper-inflammatory phase may contribute the therapeutic effects observed in our non-elderly patients.

Table 3 Cox proportional hazards models for prediction of 28-day mortality: overall patients.

Variables	Univariate Cox model			Multivariate Cox model		
	HR	(95% CI)	*P* Value	HR	(95% CI)	*P* Value
Use of corticosteroid in disease course	0.72	(0.71−2.72)	0.33	0.46	(0.22−0.97)	0.04
Secondary infection	0.53	(0.27−1.02)	0.06	0.25	(0.20−0.76)	0.006
Detection of influenza virus	1.40	(0.70−2.81)	0.34			
Underlying disease with COPD	0.81	(0.36−1.86)	0.62			
Shock in disease course	4.32	(1.89−9.90)	<0.001	2.65	(1.02−6.88)	0.05
Acute kidney injury in disease course	2.20	(1.06−4.59)	0.04	0.75	(0.32−1.74)	0.50
ARDS in disease course	7.69	(3.60−16.60)	<0.001	13.36	(5.46−32.67)	<0.001
APACHE II score ≧17	1.25	(0.60−2.60)	0.55			
CRP ≧ 5 mg/dl	1.42	(0.71−2.85)	0.32			

HR, hazard ratio; CI, confidence interval; COPD, chronic obstructive pulmonary disease; ARDS, acute respiratory distress syndrome; APACHE II, Acute Physiology and Chronic Health Evaluation II; CRP, C-reactive protein.

In recent studies, corticosteroid treatment was found to be associated with increased mortality in patients with severe influenza.[29−32] In contrast to previous findings, our subgroup analysis revealed that the use of corticosteroids in younger patients with influenza resulted in a trend of reduced mortality. The difference in study populations and corticosteroid doses may have contributed to this discrepancy. In fact, besides the aged-related immunity difference mentioned above, some studies have reported that low-to-moderate doses of methylprednisolone (25−150 mg/day or 1 mg/kg/day) improved survival in patients with severe influenza pneumonia.[28,33]; these doses were compatible with the dose in our study (median dose/day: 52 mg, dose equivalent to prednisolone). Younger patients with fewer underlying diseases than older patients may also have contributed to reduced mortality in both our study and Li's study.[28] Although a larger sample size and randomized control trials would be required, these findings suggest that the effect of corticosteroid treatment can be influenced by specific factors, including patients' age and corticosteroid dose.

Our study has several limitations. First, the type, dose, duration, and timing of corticosteroid treatment among patients were not standardized. Second, although propensity matching was performed according to key confounders, other factors, such as underlying disease, laboratory data, and vital signs on ICU admission, were not matched. However, only underlying COPD and the occurrence of ARDS during the disease course were more frequently noted in patients receiving corticosteroids. Our findings suggested that COPD was not associated with a higher in-hospital mortality rate. The occurrence of ARDS during the disease course was a risk factor associated with in-hospital mortality in both univariate and multivariate Cox regression analyses in our study; despite a significantly higher ratio being noted in the corticosteroid group, the application of corticosteroids still showed beneficial effects on the survival rate. Finally, a major limitation is the retrospective nature of this study and the lack of randomization. Therefore, only a randomized prospective trial of corticosteroid treatment can balance known and unknown factors.

Taken together, we found that corticosteroid treatment was associated with favorable 14-day and 28-day survival rates in critically ill adult patients with RV-related CAP. Such benefits were more prominent in patients younger than 70 years. Prospective, randomized, placebo-controlled trials are warranted to elucidate the therapeutic role of corticosteroids in patients with severe RV infections.

Ethical approval

This study was approved by the Institutional Review Board of Taipei Veterans General Hospital. Informed consent was not needed due to the observational nature of the study.

Author contributions

CHH: Conceptualization, formal analysis, data curation, writing - original draft, APLC: Data curation, supervision, writing - review & editing, HPC: Conceptualization, supervision, writing - review & editing. YJC: Resources, supervision, writing - review & editing.

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Declaration of competing interests

All authors declare no competing interests.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.jmii.2023.02.009.