One-Year Survival and Hospital-free Days in Critical Illness After Viral Pneumonia

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To the Editor:

Survivors of critical illness frequently suffer from persistent symptoms and impaired functional status (1, 2). Little is known on long-term outcomes from critical illness specifically related to viral pneumonia. The ability to return home and hospital-free days (HFDs) are important patient-centered outcomes (3–6). In this study, we investigated 1-year outcomes (mortality, return to home, and HFDs) in survivors who required ICU admission for seasonal influenza or coronavirus disease (COVID-19).

Data were extracted from the French National Health Data System (Système National des Données de Santé), which collects comprehensive individual pseudonymized healthcare utilization data from the entire population of 67 million inhabitants (7). The Système National des Données de Santé includes outpatient data from reimbursement claims as well as the national hospital discharge database (Program de Médicalisation des Systèmes d'Information).

We included patients ages 18 years and older who were hospitalized in a French adult ICU for at least one night for influenza (flu cohort; from January 1, 2016, to February 28, 2019) or COVID-19 (CoV cohort; January 1, 2020, to June 30, 2021). As the study focused on post-ICU outcomes, only survivors of the index ICU admission were included in the analysis. We used the Mortality-Related Morbidity Index, on the basis of 16 comorbidities identified by algorithms, to assess overall health status at baseline (8). Outcomes were mortality, return to home, and HFDs over 1 year post-ICU discharge. Patients were considered at home if alive and not hospitalized. Hospitalizations included stays in an ICU, acute care hospital, rehabilitation facility, or psychiatric ward as well as a new admission in a skilled nursing home (SNH); patients with SNH stays after the index stay were considered at home if they were already SNH residents before their index admission). HFDs were computed as days alive and not hospitalized as mentioned earlier. They were reported by age strata for all ICU survivors and for patients still alive at 1 year after ICU discharge.

We used a logistic regression model adjusted for age, sex, Mortality-Related Morbidity Index, invasive mechanical ventilation, use of vasopressors or inotropes, and renal replacement therapy during the index ICU stay to assess the association between outcome (home or deceased at 1 year) and influenza or COVID-19 among ICU survivors. Age-stratified analyses were also performed. Results are presented as percentage or median and interquartile range (IQR) or odds ratio and 95% confidence interval (CI). Analyses were performed using R Version 4.1.2.

Of the 4,470 patients who had been admitted in an ICU for at least one night with influenza, 17.6% died during their ICU stay: median age, 70 years (IQR = 63–80), 62% male, 30% with diabetes, 32% with chronic respiratory disease, 21% with heart failure, 16% with active cancer, median length of ICU stay, 10 days (IQR = 4–19), 87% with invasive mechanical ventilation, 81% with vasopressors or inotropes, 32% with renal replacement therapy, median Simplified Acute Physiology Score II, 57 (IQR = 44–73). Among patients with influenza, 3,682 were discharged alive from the ICU (flu cohort; Table 1). Of the 50,276 ICU admissions with COVID-19, 25.5% died during the index ICU stay: median age, 71 years (IQR = 65–77), 71% male, 38% with diabetes, 21% with chronic respiratory disease, 11% with active cancer, 8% with heart failure, median length of ICU stay, 14 days (IQR = 7–25), 79% with invasive mechanical ventilation, 69% with vasopressors or inotropes, 24% with renal replacement therapy, median Simplified Acute Physiology Score II, 43 (IQR = 34–54). Among patients with COVID-19, 37,441 were discharged alive from the ICU (CoV cohort; Table 1). The flu cohort was slightly older and had more comorbidities. Invasive mechanical ventilation use was similar between cohorts. More patients in the CoV cohort received noninvasive ventilation but less vasoactive drug and renal support. The median length of stay in the ICU was 50% longer in the CoV cohort.

Mortality at 1 year post-ICU discharge was 13.9% in the flu cohort versus 5.8% in the CoV cohort. These data included 3.9% and 3.1% who died in hospital after ICU discharge in the flu cohort and CoV cohort, respectively. Median time to death was 92 days (16–223) versus 22 days (6–115), respectively. Patients with COVID-19 had a lower risk of dying (death within a year: adjusted odds ratio, 0.78 [95% CI = 0.70–0.88]), except for those ages 85 years and older (1.84 [1.30–2.64]). Similar proportions returned home at least once

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Author Contributions: M. Legrand takes responsibility for the content of the article, including the data and analysis. A.A. had full access to all the data in the study and performed the statistical analysis. G.L.M., A.A., A.T., E.A., M.O.H., M.S., M. Leone, and M. Legrand contributed substantially to the study design, data analysis and interpretation, and the writing of the manuscript.

Data will not be publicly available as access is subject to prior training and authorization, and requires approval by the independent French data protection authority (Commission Nationale de l'Informatique et des Libertés, CNIL). CNAM has permanent access to SNDS data in application of provisions of article R. 1461-12 et seq. of the French Public Health code.

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Table 1. Characteristics of Patients with COVID-19 (CoV Cohort) and Patients with Influenza (Flu Cohort) Who Were Included in the Study (ICU Survivors)

Characteristic	CoV Cohort (*n* = 37,441)	Flu Cohort (*n* = 3,682)
Age category, yr, *n* (%)		
18–44	3,549 (9.5)	362 (9.8)
45–59	10,727 (28.7)	833 (22.6)
60–74	17,893 (47.8)	1,469 (39.9)
75–84	4,739 (12.7)	770 (20.9)
⩾85	533 (1.4)	248 (6.7)
Age, yr, median (IQR)	63 (54–71)	66 (56–75)
Sex, *n*		
Male	25,050 (66.9)	2,091 (56.8)
Female	12,391 (33.1)	1,591 (43.2)
Preexisting comorbidities, *n* (%)		
Heart failure	1,305 (3.5)	490 (13.3)
Cerebrovascular disease	1,114 (3.0)	236 (6.4)
Diabetes	10,219 (27.3)	1,003 (27.2)
Obesity*	5,222 (13.9)	635 (17.2)
Active cancer	1,958 (5.2)	370 (10.0)
Chronic respiratory disease	5,023 (13.4)	1,427 (38.8)
End-stage renal disease	677 (1.8)	125 (3.4)
Liver disease	785 (2.1)	176 (4.8)
Psychiatric disease	2,659 (7.1)	620 (16.8)
Dementia	211 (0.6)	98 (2.7)
MRMI, *n* (%)		
0	18,895 (50.5)	929 (25.2)
1	10,718 (28.6)	994 (27.0)
2	3,515 (9.4)	671 (18.2)
3	2,324 (6.2)	459 (12.5)
4	1,112 (3.0)	292 (7.9)
⩾5	877 (2.3)	337 (9.2)
Length of index stay, d, median (IQR)†	19 (12–33)	17 (11–29)
Length of ICU stay, d		
Median (IQR)	9 (4–18)	6 (3–12)
1–7	16,735 (44.7)	2,147 (58.3)
8–14	9,228 (24.6)	771 (20.9)
>14	11,478 (30.7)	764 (20.7)
ICU procedures, *n* (%)		
Noninvasive mechanical ventilation	28,588 (76.4)	2,464 (66.9)
Invasive mechanical ventilation	15,953 (42.6)	1,626 (44.2)
Vasopressors or inotropes	11,383 (30.4)	1,403 (38.1)
Renal replacement therapy	1,579 (4.2)	241 (6.5)
Tracheotomy	2,129 (5.7)	141 (3.8)
SAPS II, median (IQR)	33 (26–41)	38 (30–50)

Definition of abbreviations: IQR = interquartile range; MRMI = Mortality-Related Morbidity Index; SAPS II = Simplified Acute Physiology Score II.
*Identified in hospital stays with obesity or bariatric surgery.
†Including contiguous acute care hospital stays.

(flu cohort, 93.0%; CoV cohort, 95.7%). One-year post-ICU discharge, 91.9% of the CoV cohort were at home compared with 80.3% of the flu cohort (adjusted odds ratio, 1.51 [95% CI = 1.37–1.67]). The cohorts were fairly similar in terms of HFDs during the year post-ICU discharge as well as over the year prior (Figure 1). The median cumulative HFDs were 342 (287–357) and 351 (317–359) in the flu and CoV cohorts, respectively, versus 352 (337–359) and 353 (340–358), respectively, in the year before. The number of HFDs after ICU discharge fell with more advanced age in both groups.

The methodology used in our study has several strengths. This was a nationwide cohort of ICU survivors from 4 years of seasonal influenza and three waves of COVID-19. The national administrative database provides an excellent capture of healthcare trajectories and minimal loss to follow-up. Limitations include a lack of data on functional outcomes and quality of life (2). The observational design prevents any causal association. Hospital bed availability, regional resource differences, and healthcare provider preferences may have impacted healthcare trajectories and HFDs.

In summary, ICU mortality was higher in patients with COVID-19, but 1-year mortality was higher in patients who were discharged alive after influenza, except in very elderly patients. Deaths occurred later in the flu cohort compared with the CoV cohort. These differences may be related to increased age and comorbidities in

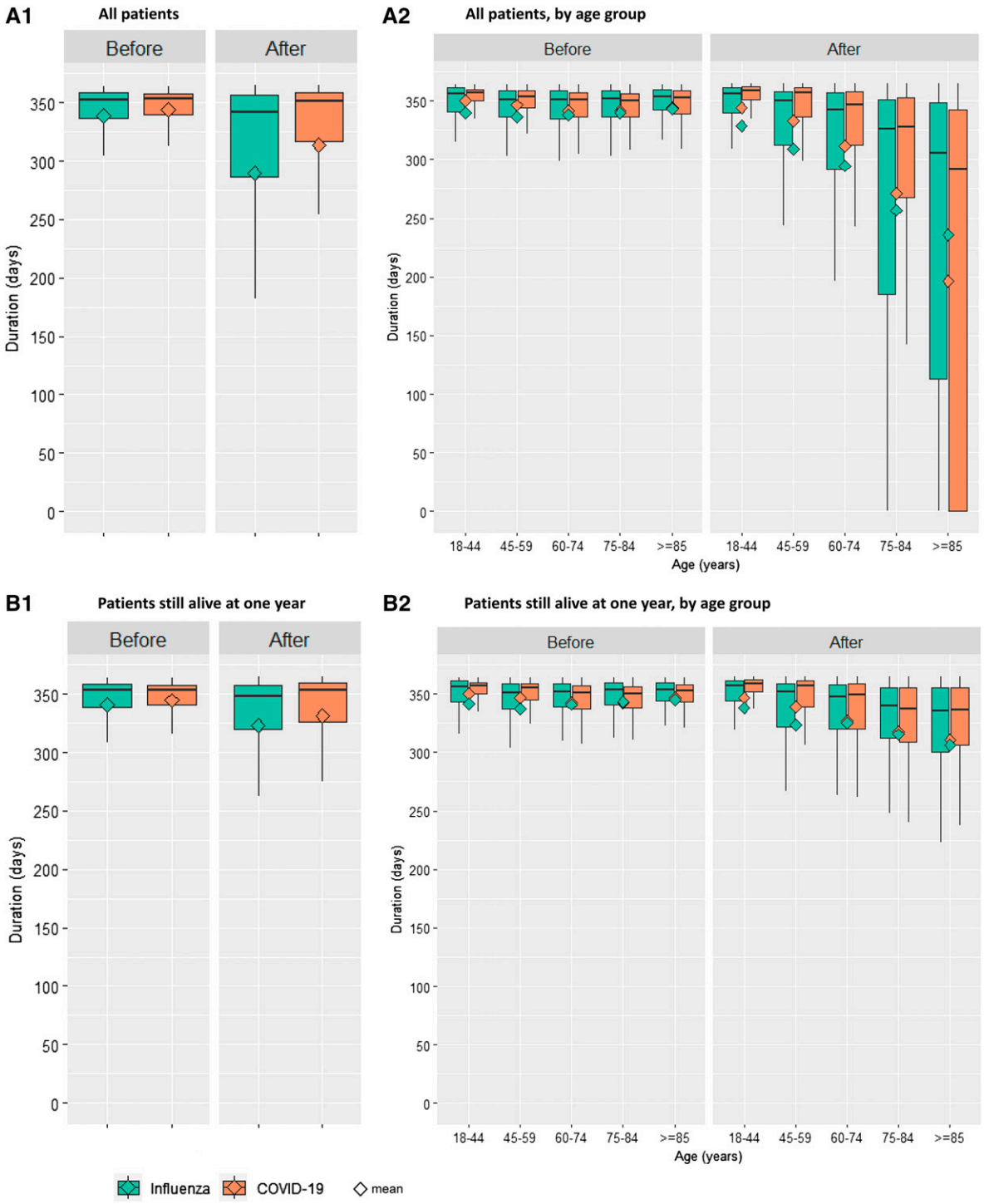

Figure 1. Distribution of the number of days spent at home (hospital-free days) during the year before and the year after ICU discharge for COVID-19 patients (CoV cohort) and influenza patients (flu cohort). (*A1* and *A2*) All patients (ICU survivors). (*B1* and *B2*) Patients who were still alive 1 year after ICU discharge. All patients, including those without any return to home (i.e., number of days at home = 0) are plotted.

the flu cohort. This aligns with previous studies showing a strong association between age, preexisting comorbidities, and postcritical illness outcomes (9). Age also alters the host response to influenza (10). Differences persisted after adjustment for these factors. Because of higher mortality, fewer patients with influenza were at home at 1 year. HFDs were, however, similar with the two viruses. To conclude, long-term outcomes among ICU survivors with influenza were similar or worse than outcomes among those with COVID. ■

Author disclosures are available with the text of this letter at www.atsjournals.org.

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Noninvasive Continuous Positive Airway Pressure Is a Lung- and Diaphragm-protective Approach in Self-inflicted Lung Injury

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To the Editor:

Strenuous spontaneous effort can promote lung and diaphragmatic injury in acute lung injury (ALI), phenomena known as "patient self-inflicted lung injury" (P-SILI) and load-induced diaphragmatic injury, respectively (1–3). Although continuous positive airway pressure (CPAP) can relieve hypoxemia and work of breathing (4), it is controversial if it prevents lung and diaphragmatic injury (5, 6). We aimed to investigate the effects of noninvasive CPAP on lung and diaphragmatic injury in an ALI model compared with unassisted animals.

Methods

The study protocol was approved by the Universidad Andrés Bello Bioethics Committee (approvals 05/2016 and 020/2017). Twenty-eight Sprague-Dawley rats weighing 270 ± 4 g were randomized to three groups: *1*) an unassisted group, representing ALI followed by unsupported spontaneous breathing ($n = 10$); *2*) a CPAP group, representing ALI followed by CPAP 6 cm H_2O

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The datasets used and analyzed during the current study are available from the corresponding author on reasonable request.

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