BRIEF REPORT

Mortality Among Noncoronavirus Disease 2019 Critically Ill Patients Attributable to the Pandemic in France

Cécile Payet, PhD[1,2]

Stéphanie Polazzi, MSc[1,2]

Thomas Rimmelé, MD, PhD[3,4]

Antoine Duclos, MD, PhD[1,2]

OBJECTIVES: We investigated whether the risk of death among noncoronavirus disease 2019 critically ill patients increased when numerous coronavirus disease 2019 cases were admitted concomitantly to the same hospital units.

DESIGN: We performed a nationwide observational study based on the medical information system from all public and private hospitals in France.

SETTING: Information pertaining to every adult admitted to ICUs or intermediate care units from 641 hospitals between January 1, 2020, and June 30, 2020 was analyzed.

PATIENTS: A total of 454,502 patients (428,687 noncoronavirus disease 2019 and 25,815 coronavirus disease 2019 patients) were included.

INTERVENTIONS: For each noncoronavirus disease 2019 patient, pandemic exposure during their stay was calculated per day using the proportion of coronavirus disease 2019 patients among all patients treated in ICU.

MEASUREMENTS AND MAIN RESULTS: We computed a multivariable logistic regression model to estimate the influence of pandemic exposure (low, moderate, and high exposure) on noncoronavirus disease 2019 patient mortality during ICU stay. We adjusted on patient and hospital confounders. The risk of death among noncoronavirus disease 2019 critically ill patients increased in case of moderate (adjusted odds ratio, 1.12; 95% CI, 1.05–1.19; $p < 0.001$) and high pandemic exposures (1.52; 95% CI, 1.33–1.74; $p < 0.001$).

CONCLUSIONS: In hospital units with moderate or high levels of coronavirus disease 2019 critically ill patients, noncoronavirus disease deaths were at higher levels.

KEY WORDS: coronavirus disease 2019; intensive care units; mortality; pandemic

Increasing numbers of coronavirus disease 2019 (COVID-19) cases seen in waves of the pandemic can rapidly overwhelm hospital capacities due to the high volume of cases mobilizing most of the available resources in healthcare staff, beds, and equipment (1, 2). Maintaining safe care for non-COVID-19 patients in this context is of major importance because excessive workload and resource prioritization toward COVID-19 cases may disorganize usual care for other patient and cause poor outcomes. We investigated whether the risk of death among non-COVID-19 critically ill patients increased when numerous COVID-19 cases were admitted concomitantly to the same ICUs or intermediate hospital units.

METHODS

Study Design and Data Source

We performed a nationwide study based on the medical information system from all public and private hospitals in France (Programme de Médicalisation

des Systèmes d'Information. Source: Agence Technique de l'Information sur l'Hospitalisation). This database is routinely used for the purpose of care reimbursement, based on accurate and exhaustive data collection process. We extracted from the hospitalization stay: patient demographics (i.e., sex and age), comorbidities according to Elixhauser algorithms (3), admission context (i.e., surgical or medical care) and reason for managing certain diseases or disorders (nervous, respiratory, circulatory, digestive, musculoskeletal, urinary and reproductive, blood, or other systems), care delivery type (i.e., ICU or intermediate care unit), the Simplified Acute Physiology Score (SAPS) II measured within the first 24 hours of admission and a selection of life-sustaining medical procedures related to organ failures (i.e., invasive ventilation, hemodynamic support, and kidney replacement therapy) at ICU admission or during the ICU stay. To define patients' socioeconomic status, the median household income of the patients' city of residence (or one of the hundred department of residence in France if the city of residence was missing in dataset) provided by the National Institute of Statistics and Economic Studies was used. The ICU beds occupancy was defined daily as the number of ICU patients over the number of ICU beds to account for change in bed capacity over time. We also considered hospital status.

This observational study was based on anonymous data and declared for ethical considerations to the National Data Protection Commission (MR-4423250520).

Study Population, Measures of Pandemic Exposure, and Outcome

All adults (patients ≥ 18 yr) admitted to ICU between January 1, 2020, and June 30, 2020, were included.

Pandemic exposure was measured daily and defined at hospital level as the proportion of COVID-19 patients among all patients treated in ICU per day (**Fig. E1**, http://links.lww.com/CCM/G613). From this definition of pandemic exposure, we defined two different variables: peak of pandemic exposure and average pandemic exposure for each non-COVID-19 patient. First, for each hospital, peak of pandemic exposure corresponded to the highest daily proportion of COVID-19 patients among all patients treated in ICU over the study period and was categorized into a three-modality variable (< 25%, between 25% and 50%, and

≥ 50%). Second, for each non-COVID-19 patient, an average pandemic exposure was specifically calculated as the mean of the daily proportion of COVID-19 patients among all patients treated in ICU during their stay and categorized into three groups according to the prespecified variable distribution: low exposure less than 25%, moderate exposure 25–50%, and high exposure greater than or equal to 50%. Therefore this average pandemic exposure definition took into account change in exposure day by day during the study period and by distinguishing that from one hospital to another.

The primary outcome was all-cause mortality during the patient stay in ICU units. COVID-19 deaths were not included in the all-cause mortality outcome measure. Inhospital mortality was also considered as a secondary outcome in sensitivity analysis.

Statistical Analysis

First, we described characteristics of non-COVID-19 patient stays according to pandemic exposure and care delivery type. Categorical variables were presented using absolute and relative frequencies, and continuous variables were presented using median, 25th and 75th percentile.

Second, we mapped the peak of pandemic exposure for each hospital in France to describe the exposure distribution across hospitals.

Finally, we computed a multivariable logistic regression model to estimate the influence of pandemic exposure on non-COVID-19 patient mortality during ICU stay. We took into account the clustering effect of patients within hospitals with the robust variance estimator (i.e., patients treated and outcomes within a particular hospital tended to be more similar than those in another hospital). The model was adjusted for potential patient confounders, including: age, sex, household income, SAPS II, Elixhauser comorbidity index, a selection of life-sustaining medical procedures related to organ failures, their hospital admission type and reason, and their stay in ICU or intermediate care unit. Additionally, we adjusted non-COVID-19 patient mortality for hospital status and ICU beds occupancy. We tested and included any significant interactions between variables in the model. The results were presented as adjusted odds ratios (ORs) with corresponding 95% CIs. Using estimated parameters obtained from this model, we determined deaths

attributable to the pandemic along with corresponding 95% CIs computed from nonparametric bootstrap based on 1,000 replications (4). We also analyzed separately admissions to ICUs and intermediate care units and performed sensitivity analyses on hospital admission related to the management of certain diseases or disorders.

All reported *p* values were two-sided, and we considered a value of less than 0.05 to be significant. Data were analyzed using SAS Version 9.4 (SAS Institute, Cary, NC).

RESULTS

A population of 454,502 patients were admitted to ICUs from 641 hospitals, including 428,687 non-COVID-19 patients (27,055 deaths). Over the study period, 186 hospitals (29.0%) experienced a peak pandemic exposure greater than 50% of patients being COVID-19 cases in their ICU beds, 174 hospitals (27.2%) a peak comprised between 25% and 50%, and 281 hospitals (43.8%) a peak not exceeding 25% (**Fig. 1**). Overall, 395,089 patients (92.2%) experienced low pandemic
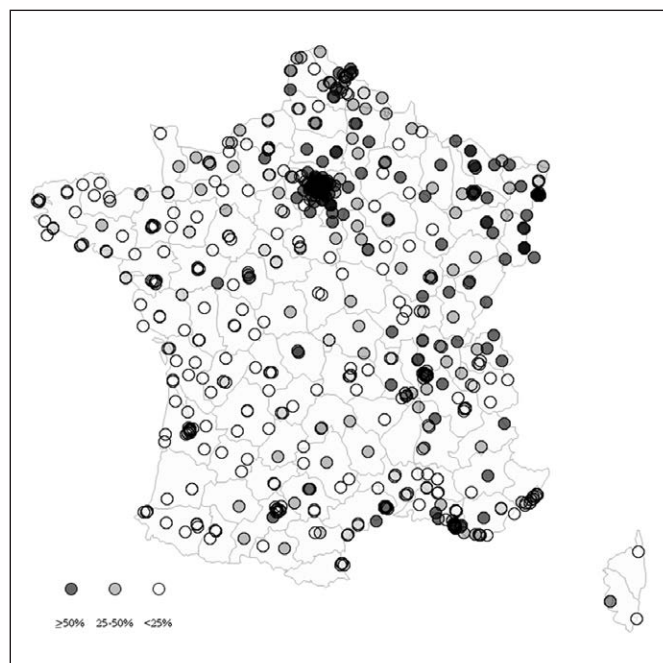

Figure 1. Hospital exposure to pandemic peak in France. We analyzed 641 hospitals in France. Every hospital's exposure to the first pandemic wave was defined as the peak proportion of coronavirus disease 2019 cases among all patients concomitantly treated in ICUs and intermediate care units. Peak pandemic exposure was less than 25% in 281 hospitals (*white*), between 25% and 50% in 174 hospitals (*light gray*), and greater than or equal to 50% in 186 hospitals (*dark gray*).

exposure during their ICU stay, 27,145 (6.3%) moderate exposure, and 6,453 (1.5%) high exposure (**Table E1**, http://links.lww.com/CCM/G613).

Mortality rate was 6.2% among non-COVID-19 patients with low pandemic exposure, 7.2% for patients with moderate exposure, and 7.7% for patients with high exposure. After adjusting for potential confounders, the risk of death among non-COVID-19 critically ill patients increased in case of moderate (adjusted OR, 1.12; 95% CI, 1.05–1.19; $p \leq 0.001$) and high pandemic exposures (1.52; 95% CI, 1.33–1.74; $p < 0.001$) (**Table 1**). This reflected a total of 378 (95% CI, 216–520) potentially deaths among non-COVID-19 patients, attributable to the pandemic. Results were consistent when analyzing separately admissions to ICUs and intermediate care units (**Table E2**, http://links.lww.com/CCM/G613), but death risk tended to be greater for patients highly exposed to pandemic in intermediate care units (1.57; 95% CI, 1.32–1.88; $p < 0.001$) than in ICUs (1.29; 95% CI, 1.08–1.55; $p = 0.006$). Similar results were found for inhospital mortality and according to different hospital admission reasons, in particular for diseases and disorders of the nervous (1.41; 95% CI, 1.17–1.69; $p < 0.001$), circulatory (1.29; 95% CI, 1.09–1.53; $p = 0.003$), and digestive (1.41; 95% CI, 1.14–1.75; $p = 0.002$) systems (**Table E3**, http://links.lww.com/CCM/G613).

DISCUSSION

Hospitals exposure to increasing numbers of COVID-19 cases observed during the first wave pandemic in France was associated with an increased risk of death among non-COVID-19 patients in need of critical care, in particular for patients admitted to intermediate care units.

A plausible explanation relates to overwhelming workload, resource prioritization, and the unanticipated creation of additional beds for managing the massive influx of COVID-19 cases. As a consequence, standard care provided to other patients may have been affected, potentially leading to safety issues with adverse events occurrence and failures to rescue (5–7). This result complement observation in the U.S. context that patients with COVID-19 in ICU had increased mortality during times of surge (8). The higher risk of death among patients admitted to intermediate units could explain because in case of overflow within ICUs, severe patients were by default admitted to

TABLE 1.
Factors Associated With Mortality Among Noncoronavirus Disease 2019 Critically Ill Patients

Factors	n = 428,687 (%)	Mortality Adjusted ORs (% CI)	p
Pandemic exposure			
Low (< 25%)	395,089 (92.2)	–	
Moderate (25–50%)	27,145 (6.3)	1.12 (1.05–1.19)	< 0.001
High (≥ 50%)	6,453 (1.5)	1.52 (1.33–1.74)	< 0.001
Patient sex			
Female	169,197 (39.5)	–	
Male	259,490 (60.5)	1.03 (0.99–1.06)	0.150
Patient age[a] (by 10 yr increase)	69.0 (57.0–79.0)	1.37 (1.34–1.40)	< 0.001
Patient SAPS II[a,b] (by 10 units increase)	19.0 (0.0–33.0)	1.89 (1.82–1.97)	< 0.001
Elixhauser comorbidity index[a]	2.0 (1.0–4.0)	1.11 (1.07–1.15)	< 0.001
Patient median household income[a], €	20.0 (18.7–21.9)	0.99 (0.99–1.00)	0.093
Hospital admission type			
Surgical care	140,988 (32.9)	–	
Medical care	287,699 (67.1)	2.19 (2.03–2.36)	< 0.001
Hospital admission reason			
Diseases and disorders of the nervous system	64,852 (15.1)	–	
Diseases and disorders of the respiratory system	53,561 (12.5)	0.76 (0.70–0.84)	< 0.001
Diseases and disorders of the circulatory system	167,170 (39.0)	0.66 (0.60–0.70)	< 0.001
Diseases and disorders of the digestive, hepatobiliary system, and pancreas	46,949 (11.0)	0.64 (0.59–0.73)	< 0.001
Diseases and disorders of the musculoskeletal system, skin, injuries, poisonings, and burns	31,145 (7.3)	0.53 (0.48–0.59)	< 0.001
Diseases and disorders of the kidney and urinary tract, reproductive systems	23,385 (5.5)	0.30 (0.26–0.34)	< 0.001
Diseases and disorders of the blood and myeloproliferative tumors	10,134 (2.4)	0.56 (0.48–0.66)	< 0.001
Others diseases and disorders	31,491 (7.3)	0.42 (0.37–0.49)	< 0.001
Care delivery type			
Intermediate care	358,251 (83.6)	–	
Intensive care	70,436 (16.4)	1.80 (1.64–1.97)	< 0.001
Invasive ventilation[c]			
No	372,122 (86.8)	–	
Yes	56,565 (13.2)	1.66 (1.54–1.80)	< 0.001
Hemodynamic support[c]			
No	364,539 (85.0)	–	
Yes	64,148 (15.0)	1.90 (1.78–2.02)	< 0.001
Kidney replacement therapy[c]			
No	418,455 (97.6)	–	
Yes	10,232 (2.4)	2.48 (2.25–2.74)	< 0.001

(*Continued*)

TABLE 1. (*Continued*).

Factors Associated With Mortality Among Noncoronavirus Disease 2019 Critically Ill Patients

Factors	n = 428,687 (%)	Mortality Adjusted ORs (% CI)	p
Hospital status			
Teaching hospital	141,770 (33.1)	–	
Public	168,458 (39.3)	1.07 (0.95–1.22)	0.268
Private	118,459 (27.6)	1.24 (1.04–1.46)	0.015
ICU beds occupancy[a] (%)	59.2 (49.6–73.8)	1.00 (0.99–1.00)	0.327
Interaction term: SAPS II × Elixhauser comorbidity index		0.96 (0.95–0.97)	< 0.001

OR = odds ratio, SAPS II = Simplified Acute Physiology Score II.

[a]Median (Q1–Q3).

[b]The SAPS II was recorded at ICU admission.

[c]Life-sustaining medical procedures related to organ failures were recorded at ICU admission or during the ICU stay.

A total of 428,687 noncoronavirus disease 2019 patients from 641 hospitals were analyzed. Using multivariable logistic regression model (with a robust error variance) accounting for patient clustering within hospitals and other confounders, we estimated adjusted ORs with their 95% CIs.

intermediate care units and could not receive optimal care. During times of surge, the threshold to be admitted into ICU beds could change toward patients who were most likely to survive and benefit from ICU resources and the most deteriorated patients could be managed upstream of ICU (9).

Available data did not allow to fully control for patient severity including the eventuality that some patients simply avoided the hospital for elective or semi-elective care with plausible concentration of complex cases which can vary across hospitals. Nevertheless, we adjusted mortality on several patient characteristics with corresponding critical care delivery, and in particular, the SAPS II to control for cases severity. We also considered hospital status and ICU beds occupancy in adjustment. However, the daily number of beds seemed to be an imperfect proxy of resources to manage patient as it did not reflect appropriately available equipment and staffing with experienced professionals. Because of potential inaccuracies inherent in medico-administrative data, we cannot rule out the possibility that residual confounders influenced our findings.

Another finding reveals noteworthy heterogeneity in pandemic exposure across the country, as half of hospitals received only a limited number of cases. Close collaborations during the wave's peak between hospitals would allow to anticipate ICU saturation and a better matching between patient needs and available healthcare staff or equipment, thus reducing mortality among both COVID and non-COVID cases (10).

CONCLUSIONS

In hospital units with moderate or high levels of COVID-19 critically ill patients, non-COVID deaths were at higher levels. This situation could be mitigated by shared strategies between hospitals for smoothing pandemic burden nationwide and better organizing patient care.

1 Research on Healthcare Performance (RESHAPE), INSERM U1290, Université Claude Bernard Lyon 1, Lyon, France.

2 Health Data Department, Lyon University Hospital, Lyon, France.

3 Department of Anesthesiology and Critical Care Medicine, Edouard Herriot Hospital, Hospices Civils de Lyon, Lyon, France.

4 Pathophysiology of Injury-Induced Immunosuppression (Pi3, EA 7426), Université Claude Bernard Lyon 1, Lyon, France.

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