Impact on disease mortality of clinical, biological, and virological characteristics at hospital admission and overtime in COVID-19 patients

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Abstract
Little is known on the association between clinical factors and coronavirus disease 2019 (COVID-19) more than 15 days after diagnosis. We conducted a multicentric prospective cohort of COVID-19 hospitalized patients to describe clinical, biological, and virological characteristics at hospital admission and over time, according to mortality up to Day 60 after admission. For the analysis of risk factors of survival, analyses assessing associations between mortality and demographic characteristics or comorbidities were performed using a Cox regression model. Between January 24 and March 15, 2020, 246 patients with reverse-transcriptase polymerase chain reactions virologically confirmed COVID-19 were enrolled. In multivariate analysis, mortality at Day 60 (n = 42 patients, 17.1% [95% confidence interval, 12.6–22.4]) was associated with older age (adjusted hazard ratio [aHR] for age ≥ 65 years: 5.22 [2.56–10.63, p < .001]), gender (aHR for male: 2.97 [1.47–5.99, p = .002]), chronic pulmonary disease (aHR: 4.84 [2.32–10.07, p < .001]), obesity (aHR: 3.32 [1.70–6.52, p < .001]), and diabetes (aHR: 1.98 [1.01–3.89, p = .048]). The median nasopharyngeal viral load at admission was 6.4 log10 copies/ml and was associated with mortality regardless of clinical risk factors. Viral load decreased with time elapsed since symptoms onset. Our study confirmed that mortality was associated with clinical characteristics at admission. The viral load at admission was significantly lower in patients admitted late after the onset of symptoms in both dead and alive patients. Our results could improve earlier identification of patients with increased risk of mortality and adapted management.

KEYWORDS
coronavirus disease 2019, emerging infection diseases, prospective cohort, SARS-CoV-2, viral load

1 | INTRODUCTION

At the end of 2019, the first cases of an epidemic of viral pneumonia of unknown etiology were reported in the city of Wuhan, China. Efficient person-to-person transmission was rapidly demonstrated. At the beginning of 2020, the Chinese health authorities and the World Health Organization (WHO) announced the discovery of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), a novel coronavirus, and its associated disease, coronavirus disease-2019 (COVID-19).1 On January 30th, WHO declared the disease as a Public Health Emergency of International Concern and, on March 11th, as a pandemic.
In France, the first confirmed case—a Chinese tourist—was reported on January 14th, 2020. As an attempt to contain the virus spread, all patients with confirmed COVID-19 were admitted to hospital, regardless of their medical condition. By March 15th, 6378 confirmed cases were reported in France, with a doubling time of 48 h. As of March 15th, admission to hospital was based on the medical condition and patients with mild symptoms were no longer hospitalized.

The national prospective French COVID cohort was initiated end-January and enrolled hospitalized patients in various centers across mainland France and overseas territories. The cohort collects systematic clinical, biological, radiological, and virological data during hospitalization, as well as after discharge. Here, we describe the clinical, biological, and virological characteristics at admission and during the first 60 days after admission in all patients enrolled up to March 15th, 2020.

2 | METHODS

2.1 | Study oversight

Hospitalized patients with a virologically confirmed COVID-19 were enrolled in the French COVID cohort (registered in clinicaltrials.gov NCT04262921). The study was conducted with the understanding and the consent of each participant or its surrogate. The study was sponsored by Inserm and Ethics approval was given by the French Ethics Committee CPP-Ile-de-France VI (ID RCB: 2020-A00256-33). All patients enrolled until March 15th, 2020 were analyzed.

2.2 | Laboratory testing for confirmation

Nasopharyngeal swabs were performed on the day of admission for SARS-CoV-2 testing according to WHO or French National Health Agency guidelines. Viral loads were quantified by real-time semi-quantitative reverse-transcriptase polymerase chain reactions (RT-PCR), using either the Charité WHO protocol (testing E gene and RdRp), or the Pasteur institute assay (testing E gene and two other RdRp targets, IP2 and IP4). When several assays were available, the IP4 Ct value was used as a reference. Results provided in cycle threshold (Ct) were transformed to log_{10} RNA copies/ml, using the relationship assessed by Pasteur Institute for both genes.

2.3 | Data collection

Data were collected through the French-modified version, the open-access Case Report Form of the International Severe Acute Respiratory and Emerging Infection Consortium. Baseline laboratory and radiological findings were recorded within the first 3 days of hospitalization. Clinical, biological, radiological, virological data, and outcomes were assessed during hospitalization. Patients were followed up 2/4 weeks after discharge and at 3 months postadmission.

2.4 | Study definitions and outcomes

The primary objectives of this study were to describe the baseline clinical, biological, and radiological characteristics of virologically-confirmed patients with COVID-19 at admission, to describe their evolution in the 60 days after admission, and to compare these variables between dead and alive patients.

2.5 | Statistical analysis

Continuous variables were described as medians and interquartile ranges [IQR]. Categorical variables were described as numbers of patients (percentages). The number of available data for each variable was given. For the analysis of risk factors of survival, univariate analyses assessing associations between mortality and demographic characteristics or co-morbidities were performed using a Cox regression model. Patients discharged alive were censored at the first date between the date of their last follow-up (date of discharge or date of visit 2-4 weeks after discharge) and the date of administrative censoring (Day 60). Variables with less than 10% of missing values and with p < .20 in univariate analysis were tested in multivariate models. The variable selection was performed using a stepwise backward multivariate Cox regression with a p-value cutoff point of .05. Two-way interactions between risk factors kept in the multivariate analysis were tested. The association between viral load (available on a subset of the population) and survival was assessed in a Cox regression multivariate model adjusted on the risk factors identified in the previous multivariate model. All tests were two-sided and analyses were performed with SAS software (SAS V9.4).

2.6 | Viral load kinetic

We assessed the association between viral load at admission and the time since symptoms onset in both dead and alive patients (Spearman’s correlation). To account for potential heterogeneity in the viral load detection, patients with Ct more than 37 were considered undetectable.

3 | RESULTS

3.1 | Demographic and clinical characteristics at admission

Among 254 eligible patients, we enrolled 246 virologically confirmed COVID-19 patients admitted to 25 hospitals, participating in the cohort throughout France (four were outpatients not hospitalized and four others had negative SARS-CoV-2 RT-PCR test results). A total of 175 (71%) patients were initially admitted to medical wards, including 27 who were subsequently transferred to the intensive care unit (ICU) or died within 60 days since admission, and 71 (29%) patients were initially admitted to ICU. The demographic and clinical characteristics of the patients at admission are shown in Table 1.
TABLE 1  Demographic, clinical, radiologic, and biologic characteristics at admission of the first 246 patients enrolled in the French COVID cohort

|                         | No.  | All N = 246 | Ward at admission (n = 175) | ICU at admission (n = 71) |
|-------------------------|------|-------------|-----------------------------|--------------------------|
| Demographic and clinical characteristics |      |             |                             |                          |
| Age: median (IQR), year | 246  | 62 [50–73]  | 60 [49–72]                  | 68 [53–76]               |
| Age distribution: no./total no. (%) | 246  |             |                             |                          |
| 15-49 year              | 59/246 (24) | 48/175 (27) | 11/71 (15)                 |
| 50-64 year              | 81/246 (33) | 59/175 (34) | 22/71 (31)                 |
| 65-80 year              | 73/246 (30) | 46/175 (26) | 27/71 (38)                 |
| ≥80 year                | 33/246 (13) | 22/175 (13) | 11/71 (15)                 |
| Male sex: no./total no. (%) | 246  |             |                             |                          |
| Arab                    | 14/162 (9)  | 6/112 (5)   | 8/50 (16)                  |
| Black                   | 15/162 (9)  | 8/112 (7)   | 7/50 (14)                  |
| Asian                   | 8/162 (5)   | 4/112 (4)   | 4/50 (8)                   |
| White                   | 118/162 (73)| 88/112 (79)| 30/50 (60)                 |
| Healthcare worker: no./total no. (%) | 246  |             |                             |                          |
| Smoking history: no./total no. (%) | 169  |             |                             |                          |
| Never smoked            | 113/169 (67) | 81/121 (67) | 32/48 (67)                 |
| Former smoker           | 43/169 (25) | 30/121 (25) | 13/48 (27)                 |
| Current smoker          | 13/169 (8)  | 10/121 (8)  | 3/48 (6)                   |
| Comorbidities: no./total no. (%) |      |             |                             |                          |
| At least one comorbidity| 239  | 148/239 (38) | 93/169 (45) | 55/70 (21) |
| Chronic cardiac disease (not hypertension) | 245  | 48/245 (20) | 32/174 (18) | 16/71 (23) |
| Hypertension            | 243  | 73/243 (30) | 42/173 (24) | 31/70 (44) |
| Chronic pulmonary disease (not asthma) | 246  | 21/246 (9)  | 12/175 (7)  | 9/71 (13)  |
| Asthma                  | 246  | 23/246 (9)  | 14/175 (8)  | 7/71 (10)  |
| Chronic kidney disease  | 246  | 16/246 (7)  | 7/175 (4)   | 9/71 (13)  |
| Chronic liver disease   | 245  | 9/245 (4)   | 8/175 (5)   | 1/70 (1)   |
| Chronic neurological disorder | 246  | 18/246 (7)  | 10/175 (6)  | 8/71 (11)  |
| Malignant neoplasm      | 245  | 14/245 (6)  | 11/175 (6)  | 3/70 (4)   |
| Chronic hematologic disease | 246  | 8/246 (3)   | 6/175 (3)   | 4/71 (6)   |
| AIDS/HIV                | 74   | 0/74 (0)    | 0/50 (0)    | 0/24 (0)   |
| Obesity                 | 241  | 44/241 (18) | 17/171 (10) | 27/70 (39) |
| Diabetes                | 244  | 39/244 (16) | 26/175 (15) | 13/69 (19) |
| Rheumatologic disorder  | 244  | 20/244 (8)  | 11/173 (6)  | 9/71 (13)  |
| Dementia                | 246  | 5/246 (2)   | 4/175 (2)   | 1/71 (1)   |
| Malnutrition            | 244  | 1/244 (0)   | 1/173 (1)   | 0/71 (0)   |
| Splenectomy             | 245  | 0/245 (0)   | 0/175 (0)   | 0/70 (0)   |
| Sickle cell disease     | 178  | 0/178 (0)   | 0/131 (0)   | 0/47 (0)   |
| Solid organ transplant  | 242  | 3/242 (1)   | 2/174 (1)   | 1/68 (1)   |
| Inflammatory bowel disease | 240  | 4/240 (1)   | 4/172 (2)   | 0/0 (0)    |
| Immunosuppressive therapy: no./total no. (%) |      |             |                             |                          |
| Corticoid               | 245  | 8/245 (3)   | 4/175 (2)   | 4/70 (6)   |
| Number of days with symptoms before admission: median (IQR) | 243  | 6 [3–8]     | 5 [3–8]     | 7 [4.5–9]  |
| Clinical characteristics at admission: no./total no. (%) |      |             |                             |                          |
| Cough                   |      |             |                             |                          |
| With sputum production  | 219  | 40/219 (18) | 29/160 (18) | 11/59 (19) |
| With hemoptysis         | 221  | 2/221 (1)   | 2/161 (1)   | 0/60 (0)   |

(Continues)
| TABLE 1 (Continued) |
|---------------------|
| **No.** | **All N = 246** | **Ward at admission (n = 175)** | **ICU at admission (n = 71)** |
| Sore throat | 218 | 31/218 (14) | 30/166 (18) | 1/52 (2) |
| Runny nose | 226 | 46/226 (20) | 44/171 (26) | 2/55 (4) |
| Ear pain | 190 | 3/190 (2) | 2/153 (1) | 1/37 (3) |
| Wheezing | 229 | 15/229 (7) | 6/171 (4) | 9/58 (16) |
| Chest pain | 231 | 22/231 (10) | 18/172 (10) | 4/59 (7) |
| Myalgia | 232 | 96/232 (41) | 78/171 (46) | 18/61 (30) |
| Arthralgia | 225 | 24/225 (11) | 19/168 (11) | 5/57 (9) |
| Faintness | 225 | 124/225 (55) | 96/167 (57) | 28/60 (47) |
| Shortness of breath | 241 | 108/241 (45) | 51/173 (29) | 57/68 (84) |
| Headache | 233 | 71/233 (30) | 68/171 (40) | 5/63 (8) |
| Altered consciousness/confusion | 238 | 11/238 (5) | 6/175 (3) | 5/63 (8) |
| Seizures | 234 | 24/234 (11) | 19/168 (11) | 5/57 (9) |
| Abdominal pain | 235 | 14/235 (6) | 8/172 (5) | 6/63 (10) |
| Vomiting/nausea | 238 | 26/238 (11) | 19/174 (11) | 7/64 (11) |
| Diarrhea | 239 | 45/239 (19) | 34/173 (20) | 11/66 (17) |
| Conjunctivitis | 237 | 4/237 (2) | 4/173 (2) | 0/64 (0) |
| Skin rash | 239 | 4/239 (2) | 2/175 (1) | 2/64 (3) |
| Skin ulcers | 201 | 0/201 (0) | 0/155 (0) | 0/64 (0) |
| Lymphadenopathy | 235 | 3/235 (1) | 2/172 (1) | 1/63 (2) |
| Anosmia | 109 | 5/109 (5) | 4/76 (5) | 1/33 (3) |
| Ageusia | 110 | 4/110 (4) | 3/77 (4) | 1/33 (3) |
| Hemorrhage | 238 | 1/238 (0) | 1/174 (1) | 0/64 (0) |
| Fever: no./total no. (%) | 235 | 84/235 (36) | 46/170 (27) | 38/65 (58) |
| Heart rate: median (IQR), beats per min | 221 | 85 [77–97] | 84 [75.25–98.75] | 87 [80–95.5] |
| Respiratory rate: median (IQR), breaths per min | 108 | 20 [16–26] | 19 [16–20] | 25 [22–30] |
| Systolic blood pressure: median (IQR), mmHg | 224 | 130 [118–140] | 130 [120–140] | 128 [113–138] |
| Diastolic blood pressure: median (IQR), mmHg | 224 | 77 [65–85] | 78 [68–86] | 70 [62–81] |
| Severe dehydration: no./total no. (%) | 201 | 7/201 (3) | 5/145 (3) | 2/64 (3) |
| Oxygen saturation on room air: median (IQR), % | 152 | 96 [94–98] | 96 [95–98] | 90 [81.5–93.75] |
| Oxygen therapy: no./total no. (%) | 214 | 61/214 (29) | 14/148 (9) | 47/66 (71) |
| Oxygen flow: median (IQR), L/min | 15 | 2 [0–8] | 0 [0–1.125] | 8 [4–15] |
| Coinfections: no./total no. (%) | | | | |
| Influenza | 189 | 3/189 (2) | 2/127 (2) | 1/62 (2) |
| Adenovirus | 212 | 0/162 (0) | 0/103 (0) | 0/59 (0) |
| Bacteria | 168 | 10/168 (6) | 4/106 (4) | 6/62 (10) |
| Viral load (log_{10} copies/ml) | 184 | 6.6 [4.2–8.6] | 6.7 [4.4–8.6] | 6.2 [4.1–8.4] |
| Radiologic findings in the first 3 days following first positive SARS-CoV-2 sample | | | | |
| Abnormalities on chest radiograph: no./total no. (%) | 239 | 103/131 (78.6) | 44/71 (62) | 59/60 (98.3) |
| Alveolar opacity | 238 | 49/95 (51.6) | 20/44 (45.5) | 29/51 (56.9) |
| Interstitial infiltration | 243 | 90/100 (90) | 40/44 (90.9) | 50/56 (89.3) |
| Pleural effusion | 239 | 3/96 (3.1) | 2/43 (4.7) | 1/53 (1.9) |
| Pneumothorax | 238 | 2/95 (2.1) | 1/43 (2.3) | 1/52 (1.9) |
| Bilateral | 241 | 83/98 (84.7) | 32/44 (72.7) | 51/54 (94.4) |

Laboratory findings in the first 3 days following first positive SARS-CoV-2 sample

| Hemoglobin: median (IQR), g/dL | 88 | 13.4 [12.5–14.5] | 13.9 [13–14.5] | 12.5 [11.6–13.5] |
| WBC count: median (IQR), ×10^9/L | 92 | 5.6 [4.3–7.5] | 5.4 [4.1–6.7] | 6.4 [5–8.9] |
The median age was 62 years (IQR, 50–73), with 106 (43%) aged 65 years or older, and the proportion of males was 57%. The proportion of patients having at least one comorbidity was 38%, in particular hypertension (30%), other chronic cardiovascular diseases (20%), obesity (17%), and diabetes (16%). The proportion of current smokers was 8%. The proportion of healthcare workers or working in a microbiology laboratory was 9%. The median number of days between the onset of clinical symptoms until hospital admission was 7 days.5–11 The four most common symptoms at admission were a history of fever, faintness, shortness of breath, and myalgia. Chest x-ray at admission was abnormal in 75% of the patients, with bilateral abnormalities in 82% of them. Laboratory findings at the admission are summarized in Table 1.

### 3.2 | Follow-up and outcome at Day 60 postadmission

Figure 1 shows the evolution of all patients during the first 60 days after admission. At Day 60, 42 patients had died (17.1% [95% confidence interval [CI], 12.6–22.4]), 192 had been discharged alive (78.0% [72.3–83.1]), eight were still hospitalized in medical wards (3.3% [1.4–6.3]), and four were still hospitalized in ICU (1.6% [0.4–4.1]). The survival curve is shown in Figure S2. Of the 175 patients initially admitted to medical wards, 27 patients worsened and were subsequently transferred to ICU or died (15.4% [10.4–21.6]). Overall, 12 patients initially admitted to medical wards died (6.9% [3.6%–11.7%]) and 30 patients initially admitted to ICU died (42.3% [30.6%–54.6%]; Figure S1). Of note, no patient initially admitted to medical wards was transferred to ICU after Day 14; however, the mortality rate was different between Day 14 (25/246, 10.2% [6.7–14.6]) and Day 60 (42/246, 17.1% [12.6–22.4]).

During hospitalization, patients were treated at the doctor’s discretion as follows: 9/241 (4%) with remdesivir (7/200 in alive patients at D60 and 2/41 in dead patients at D60), 5/194 (3%) with hydroxychloroquine (3/156 in alive patients at D60 and 2/38 in dead patients at D60), and 68/241 (27%) with lopinavir/ritonavir (50/200 in alive patients at D60 and 18/41 in dead patients at D60). Figure 2 shows the evolution of selected clinical and biological parameters. Patients who subsequently died had higher heart and respiratory rates at admission, and these values continued to increase during follow-up as compared with alive patients. Likewise, C-reactive protein (CRP), blood urea nitrogen, and white blood cells count increased more rapidly during the first week of hospitalization in patients who subsequently died than in those who survived. Hemoglobin decreased rapidly in the first week of follow-up while platelet count sharply dropped later on in patients who subsequently died compared to those who survived.

### 3.3 | Comparison of demographic and comorbidities at admission between dead and alive patients

We compared baseline demographic and comorbidities between dead (n = 42) and alive (n = 204) patients. In univariate analysis (Table 2), older age, male gender, chronic cardiac disease, hypertension, chronic pulmonary disease, chronic kidney disease, chronic neurological disorder, malignant neoplasm, obesity, and diabetes were significantly associated with severe disease. In multivariate analysis, older age (aHR for age ≥ 65 years: 5.22 [2.56–10.63, p < .001]), gender (aHR for male: 2.97 [1.47–5.99, p = .002]), chronic pulmonary disease (aHR: 4.84 [2.32–10.07, p < .001]), obesity (aHR: 3.32 [1.70–6.52, p < .001]), and diabetes (aHR: 1.98 [1.01–3.89,
\( p = .048 \) were independent risk factors associated with mortality. There was no significant two-way interaction among those factors. Viral load at admission was associated with mortality adjusted on the previous five clinical risk factors (Table S1).

### 3.4 Viral loads

A total of 351 nasopharyngeal viral load data were obtained from 159 patients, with 35 dead patients and 124 alive patients at Day 60 (Figure 3A). The median viral load at admission was 6.4 log10 copies/ml [IQR, 4.2–8.6]. The viral load at admission was significantly lower in patients admitted late after the onset of symptoms in both dead and alive patients \( (p = .06 \) and \( P < 10^{-4} \), respectively, Figure 3B).

### 4 DISCUSSION

In this prospective clinical cohort, we described the clinical, biological, and virological characteristics at admission and during the first 60 days of hospitalization in all patients enrolled up to March 15th, 2020. Other studies comparing characteristics of patients with and without severe diseases have been published recently in larger populations, in particular in the United States and in China.\(^7,8\) However, these studies were mostly retrospective or studies in which data were collected retrospectively, and many of these data were restricted to critical or severe patients, with a short-term follow-up and no data on viral load kinetics. For example, a retrospective report was published on more than 1500 patients in Lombardia, Italy, but this study only included ICU patients.\(^9\) In the present study, we prospectively enrolled patients with a wide range of disease severity status: patients who did not medically require hospitalization but who were hospitalized to avoid disease transmission in the community, patients who required hospitalization but who were not admitted to ICU, and those admitted to ICU. This allows us to evaluate characteristics associated with mortality and with a pre-planned and prospective collection of biological and virological data.

The mortality rate at Day 60 was 17.1% [12.6–22.4%], which is lower than in larger series, such as those published from New York City area (21%)\(^8\) and Wuhan (28%).\(^10\) Also, in the RECOVERY trial, overall 28-day mortality was 25.7% in the usual care group.\(^11\) This might be due, in part, to the enrollment of patients with mild COVID-19 disease who were hospitalized at the very beginning of the epidemic in France. Indeed, again in the RECOVERY trial, 28-day mortality was 17.8% and 14.0% for the dexamethasone group and the usual care group, respectively, in patients who did not require oxygen at the time of randomization.\(^11\) Interestingly, the mortality rate was 10.2% [6.7–14.6] at Day 14 and rose up to 17.1% [12.6–22.4] at Day 60. Of note, no patient initially admitted to medical wards was transferred to ICU after Day 14 postadmission, suggesting delayed death in those admitted/transfered to ICU. In our study, 30% of patients had hypertension and 17% were obese, as compared with 57% and 42% in papers from the New York City area.\(^8\) These numbers are close to estimates from the French general population.
with prevalence rates of 30.6% and 15.7%, respectively. Accordingly, the prevalence of diabetes (16%) was close to that in the general population, with a prevalence of 16% as compared with 20% in men aged between 75 and 85 years in the French general population. The proportion of current smokers was equal to 8%, which is much lower than in the French general population, in the range 25%-30%. This proportion is nonetheless highly age-dependent and falls to 20% in people aged between 55 and 64 years, and to 10% in those aged between 65 and 75 years.

Age, male gender, chronic pulmonary disease (not asthma), obesity, and diabetes were associated with mortality, in line with previous reports. Cardiovascular comorbidities, such as chronic cardiac disease, were associated with mortality in the univariate analysis but not in the multivariate analysis, possibly due to confounding factors, such as obesity and diabetes.

We compared the dynamics of clinical and biological variables over time in dead and alive patients. An increase in respiratory rate, in heart rate and/or biological parameters, in particular CRP, white blood count, and in blood urea nitrogen, and a drop in platelet count were early predictive markers of subsequent death and could be useful in the future to guide clinicians.

One of the strengths of this cohort was to collect nasopharyngeal viral load measurements at admission and prospectively.
A striking observation was that viral load at admission decreased with the time since symptom onset, with an association with mortality adjusted on clinical risk factors.

Our study has certain limitations. The epidemic situation linked to COVID-19 in France did not allow for an optimal data collection, leading to several missing data. Although patients from various geographical places in France were enrolled, most of the participating centers were University hospitals in which the proportion of most severe patients tends to be larger.

We systematically and prospectively collected data, including clinical, biological, and virological on 246 patients and found several risk factors of mortality. The results of this analysis could improve our knowledge of clinical and biological characteristics associated with disease evolution, thus improving medical care through better

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**TABLE 2** Demographic and baseline comorbidities associated with time to death until Day 60, in the first 246 patients enrolled in the French COVID cohort

| Demographic and clinical characteristics | Missing n (%) | Alive (n = 204) | Dead (n = 42) | Bivariate HR (95%CI) | p | Multivariate aHR (95% CI) (n = 239–197) | p |
|------------------------------------------|--------------|----------------|-------------|---------------------|---|----------------------------------------|---|
| Age: median (IQR), year                  | 0 (0)        | 59 [47.75–70]  | 74 [65.5–80.75] | 1.06 (1.04–1.09)    | <.001 |                                      |   |
| Age distribution: no./total (%)          | 0 (0)        | 62/204 (30)    | 2/42 (5)    | 1                  | 1 |                                        |   |
| 15–49 year                               | 0 (0)        | 73/204 (36)    | 7/42 (17)   | 2.67 (0.55–12.85)   | .22 |                                        |   |
| 65–80 year                               | 16/204 (8)   | 21/42 (50)     | 12/42 (29)  | 18.08 (4.04–80.84)  | <.001 |                                      |   |
| Male sex: no./total no. (%)              | 0 (0)        | 108/204 (53)   | 31/42 (74)  | 2.32 (1.17–4.62)    | .02 | 2.97 (1.47–5.99)                       | .002 |
| Ethnic group: no./total no. (%)          | 84 (34)      |                |            |                     |    |                                        |   |
| Arab                                     | 9/128 (7)    | 5/34 (15)      | 2.18 (0.82–5.77) | .12 |                                      |   |
| Black                                    | 12/128 (9)   | 3/34 (9)       | 0.99 (0.3–3.32) | .99 |                                      |   |
| Asian                                    | 5/128 (4)    | 3/34 (9)       | 1.92 (0.57–6.47) | .29 |                                      |   |
| White                                    | 96/128 (75)  | 22/34 (65)     | 1           |                                        |   |
| Healthcare worker: no./total no. (%)     | 0 (0)        | 21/204 (10)    | 1/42 (2)    | 0.21 (0.03–1.53)    | .12 |                                        |   |
| Smoking history: no./total no. (%)       | 77 (31)      |                |            |                     |    |                                        |   |
| Never smoked                             | 95/140 (68)  | 18/29 (62)     | 1           |                                        |   |
| Former smoker                            | 34/140 (24)  | 9/29 (31)      | 1.44 (0.65–3.22) | .37 |                                      |   |
| Current smoker                           | 11/140 (8)   | 2/29 (7)       | 1.36 (0.31–5.86) | .68 |                                        |   |
| Comorbidities: no./total no. (%)         |              |                |            |                     |    |                                        |   |
| Chronic cardiac disease (not hypertension) | 1 (0.4)    | 31/203 (15)    | 17/42 (40)  | 3.65 (1.97–6.77)    | <.001 |                                      |   |
| Hypertension                             | 3 (1)        | 48/201 (24)    | 25/42 (60)  | 3.77 (2.04–6.99)    | <.001 |                                      |   |
| Chronic pulmonary disease (not asthma)   | 0 (0)        | 10/204 (5)     | 11/42 (26)  | 5.33 (2.67–10.62)   | <.001 | 4.84 (2.32–10.07)                      | <.001 |
| Asthma                                   | 17/204 (8)   | 4/42 (10)      | 1.17 (0.42–3.28) | .77 |                                      |   |
| Chronic kidney disease                   | 9/204 (4)    | 4/42 (19)      | 4.7 (2.17–10.16) | <.001 |                                      |   |
| Chronic liver disease                    | 7/203 (3)    | 2/42 (5)       | 1.28 (0.31–5.28) | .74 |                                      |   |
| Chronic neurological disorder            | 10/204 (5)   | 8/42 (19)      | 4.11 (1.9–8.89) | <.001 |                                      |   |
| Malignant neoplasm                       | 1 (0.4)      | 9/204 (4)      | 5/41 (12)   | 3.05 (1.19–7.78)    | .02 |                                        |   |
| Chronic hematologic disease              | 6/204 (3)    | 4/42 (10)      | 2.49 (0.89–6.99) | .08 |                                      |   |
| Obesity                                  | 30/199 (15)  | 14/42 (33)     | 2.34 (1.23–4.44) | .009 | 3.32 (1.70–6.52)                      | <.001 |
| Diabetes                                 | 26/202 (13)  | 13/42 (31)     | 2.43 (1.26–4.67) | .008 | 1.98 (1.01–3.89)                      | .048 |
| Rheumatologic disorder                   | 2 (0.8)      | 15/202 (7)     | 5/42 (12)   | 1.66 (0.65–4.23)    | .29 |                                        |   |

Abbreviation: COVID, coronavirus disease.

*aHR: hazard ratios of the association of each factor with mortality.

baHR: adjusted hazard ratios of the association with mortality.
triage, earlier identification of patients with increased risk of mortality, and adapted management.

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FIGURE 3 Viral load kinetics in 159 patients out of the first 246 of the French COVID cohort in which at least one viral load was available. (A) Nasopharyngeal viral load. (B) Viral load at admission according to the time since symptom onset. Light blue: not deceased patients; orange: deceased patients. COVID, coronavirus disease.
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CONFLICT OF INTEREST
Pr. Yazdanpanah reports no conflict of interest.

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