Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Elsevier hereby grants permission to make all its COVID-19-related research that is available on the COVID-19 resource centre - including this research content - immediately available in PubMed Central and other publicly funded repositories, such as the WHO COVID database with rights for unrestricted research re-use and analyses in any form or by any means with acknowledgement of the original source. These permissions are granted for free by Elsevier for as long as the COVID-19 resource centre remains active.
Original Article

Effect of SARS-CoV-2 infection and pandemic period on healthcare-associated infections acquired in intensive care units

Alain Lepape 1,2,3,*, Anaïs Machut 2,4, Cedric Bretonnière 2,5, Arnaud Friggeri 1,2,3, Charles-Hervé Vacheron 1,2, Anne Savey 2,3,4, on behalf of REA-REZO network

1) Service d’anesthésie, de Médecine Intensive, de Médecine péri-opératoire et de Réanimation Hospices Civils de Lyon Groupement Sud, Lyon, France
2) REA-REZO (Surveillance, Infections & Antibiotic Resistance Network in ICU), Hospices Civils de Lyon Groupement Sud, St Genis Laval, France
3) Public Health, Epidemiology and Evolutionary Ecology of Infectious Diseases, Centre International de Recherche en Infectiologie Lyon, France
4) CHU Clermont-Ferrand, Génétique et Biologie Moléculaire, Clermont-Ferrand, France
5) Unité des Soins Intensifs de Pneumologie, Institut du Thorax, Nantes CHU, Nantes, France

ARTICLE INFO

Article history:
Received 21 June 2022
Received in revised form 11 October 2022
Accepted 16 October 2022
Available online xxx

Editor: L. Scudeller

Keywords:
COVID-19
Hospital-acquired infections
Intensive care
Surveillance network
Ventilator-associated pneumonia

ABSTRACT

Objectives: To compare the occurrence of healthcare-associated infections acquired in intensive care units (HAI-ICUs) in France among patients with COVID-19 and those with it in 2020 and the latter with that in patients before the COVID-19 pandemic.

Methods: Multicentre HAI-ICU surveillance network (REA-REZO) data were used to identify 3 groups: 2019 patients (2019Control), a COVID-19 group (2020Cov), and a non-COVID-19 group (2020NonCov). The primary outcome was the occurrence of HAI-ICU (ventilator-associated pneumonia [VAP], bloodstream infections [BSIs], catheter-related bacteraemia). Standardized infection ratios of VAP were calculated for each quarter in 2020 and compared with those in 2019.

Results: A total of 30,105 patients were included in 2020: 23,798 in the 2020NonCov group, 4,465 in the 2020Cov group, and 39,635 patients in the 2019Control group. The frequency of VAP was strikingly greater in the 2020Cov group: 35.6 (33.4–37.8) episodes/1000 days of mechanical ventilation versus 18.4 (17.6–19.2) in the 2020NonCov group. VAP standardized infection ratio was high in 2020 patients, particularly during the 2 quarters corresponding to the 2 waves. BSI/1000 days were more frequent in the 2020Cov group than in the 2019Control group. The microbial epidemiology was only slightly different.

Discussion: The data presented here indicate that HAI-ICUs were more frequent during the COVID-19 period, whether the patients were admitted for COVID-19 or, to a lesser extent, for another cause. This implies that managing patients with severe disease in a pandemic context carries risks for all patients.

© 2022 European Society of Clinical Microbiology and Infectious Diseases. Published by Elsevier Ltd. All rights reserved.

Introduction

In France, and worldwide, intensive care units (ICUs) have been the main battleground to treat patients with severe COVID-19 that is associated with a high risk of death [1]. The pandemic had a major effect on the hospital organization, with work overload, creation of temporary beds in ICUs, involvement of personnel not usually dedicated to ICUs, and an initial shortage of personal protective equipment [2]. This situation was further complicated by the continuous flow of patients in ICU without COVID-19. REA-REZO is a nationally active surveillance network dedicated to the epidemiology of ICU-acquired infections as well as the use of antimicrobials and bacterial epidemiology running since 2004 in voluntary French ICUs [3–5]. During the COVID-19 pandemic period, the ongoing surveillance programme was continued on the same basis with the identification of patients with COVID-19. The objective of the study was to compare first the occurrence of healthcare-associated infections acquired in ICUs (HAI-ICUs) in 2020 patients with COVID-19 with that in 2020 patients without COVID-19, and secondly the latter with that in 2019 patients before the COVID-19 pandemic.

* Corresponding author. Service d’anesthésie, de médecine intensive, de médecine péri-opératoire et de réanimation Hospices Civils de Lyon Groupement Sud, Lyon France Hospices Civils de Lyon Groupement Sud 165 Chemin du Grand Revoyet, F69405 Pierre-Bénite, France.
E-mail address: alain.lepape@chu-lyon.fr (A. Lepape).

https://doi.org/10.1016/j.cmi.2022.10.023
1198-743X/© 2022 European Society of Clinical Microbiology and Infectious Diseases. Published by Elsevier Ltd. All rights reserved.
Methods

Surveillance design

The continuous surveillance is carried out in ICUs on a voluntary basis and is patient-based, including each patient with a length of stay ≥2 calendar days in an adult ICU. Individual data were prospectively recorded on HAIs, with selected antimicrobial resistance and individual risk factors (Table S1). The database was approved by the National Data Protection Commission (Commission nationale de l’informatique et des libertés, Number 919149) and by the institutional review board (CPP SUD EST—IRB 00009118). The protocol is available on the website of the network [6].

Surveillance data

General patient characteristics

Age, sex, severity as assessed by the Simplified Acute Physiological Score II [7], date of ICU admission and discharge, status at ICU discharge (alive or deceased), antibiotic treatment (excluding prophylaxis) ± 2 days before or after admission day, category of diagnosis (medical, surgical scheduled or emergency, and trauma), origin of the patient (community, long-term care, rehabilitation centre, acute care, and other ICU), and immunosuppression were recorded.

Individual exposure to invasive device

The dates of insertion and removal of the endotracheal tube and central venous catheter (CVC) as well as the site of CVC insertion were recorded.

Healthcare-associated infections acquired in intensive care units

Pneumonia, including ventilator-associated pneumonia (VAP), catheter-related bacteraemia (CRB), as well as bloodstream infections (BSIs) of all origins were recorded. Pulmonary infection data included the date of onset and the method of diagnosis of pneumonia.

For each infection, up to 2 microorganisms were recorded, as well as resistance status by tracer phenotypes for bacteria of interest (Staphylococcus aureus, Enterococcus faecalis and Enterococcus faecium, Enterobacterales, Pseudomonas aeruginosa, and Acinetobacter sp.; (Table S1). Susceptibility testing in all units was performed according to the European Committee on Antimicrobial Susceptibility Testing [8].

Definitions of ICU-acquired infections

HAIs are infections occurring >48 hours after admission. Definitions follow the European Centre for Disease Control definitions [9].

Briefly, pneumonia is defined by a combination of clinical, radiological, and laboratory criteria. VAP is a lung infection in a patient mechanically ventilated for >48 hours. BSIs are defined by the positivity of at least one blood culture for a recognized pathogen or two positive blood cultures for a common skin contaminant. The complete definition set can be found on the European Centre for Disease Control Website [10].

The outcomes include the incidence of HAI expressed as incidence, as well as incidence density per 1000 patient-days for BSI and per 1000 days of device exposure for specific infections (mechanical ventilation for VAP and catheter for CRB).

Surveillance design

The data collection was performed using a standardized form completed for each patient by the physician in charge in collaboration with the Infection Control Unit; the data collected concerns patient characteristics, devices used, and HAI. These data were collected during the ICU stay, and the form was finalised at the end of the ICU stay, for each patient staying 2 or more days.

Statistical plan

Descriptive statistics were expressed by the median and interquartile range for quantitative variables and by the number and percentage (%) for qualitative variables. The device utilization ratio was calculated by dividing the total number of device days by the total number of patient-days during the stay. Differences among the groups were estimated using the Wilcoxon rank-sum test for quantitative variables and the chi-square test for qualitative variables or Fisher exact test when applicable. If heterogeneity among groups was detected, a two-by-two comparison was performed to detect the group differences. The statistical threshold for between-group comparisons was set at 0.001.

Standardized infection ratios (SIRs) were computed as previously described [11]: the proportion of change (%) in VAP incidence was calculated as follows: [(2020 SIR − 2019 SIR) / 2019 SIR] × 100. Temporal comparisons in VAP incidence between 2019 and 2020 were analysed using SIR, calculated for each calendar quarter by dividing the number of reported infections by the number of predicted infections. A SIR >1 indicates fewer infections observed than predicted; likewise, a SIR <1 indicates that more infections were observed than predicted. The predicted individual probability of occurrence of VAP was estimated using logistic regression: first, a backward stepwise regression was performed to select the best minimal model to explain a VAP using a subset of predefined variables (Table S2). The model fit was maximized using the minimal Akaike information criterion. The OR and their 95% CI were computed for the variables retained in the final model. Analyses were performed using the SAS-Studio (SAS Institute Inc., Cary, NC).

Results

Population

The number of participating units was N = 110 in 2019 and N = 90 in 2020. In 2020, 30 105 patients were reported in the surveillance network database: 23 798 patients in the non-COVID-19 (2020NonCov) group; 4465 patients in the COVID-19 (2020Cov) group, including 3800 patients with COVID-19 diagnosed by PCR and 665 on clinical basis (mainly before complete accessibility of PCR early in the year 2020). However, 1842 patients with an unknown COVID-19 status were not included in the present study. In 2019, 39 635 patients were included in the surveillance (Fig. 1).

Patient characteristics

The 2019Control and 2020NonCov patients were comparable, except for the proportion of scheduled surgical patients who were low in the 2020NonCov group. A greater proportion of patients in the 2020Cov group was transferred from a ward or other ICU than patients in the 2020NonCov. According to the number of 2020Cov and 2020NonCov admissions each month in 2020, there were 2 waves in France: the first in March, the second in October–November (Fig. S1). The median length of ICU stays, sex ratios, and fatality rates were greater in the 2020Cov group than in the 2020NonCov group. Exposure to antibiotics was not different between the 2019Control and the 2020NonCov population, but higher in the 2020Cov group than in the 2020NonCov group (Table 1).

Exposure to invasive devices (endotracheal tube or CVC) was slightly increased in the 2020NonCov group. The exposure duration and the device utilization ratio were higher in the 2020Cov group.
During 2020, the proportion of intubated patients decreased among the patients in the 2020Cov group and remained stable in the patients in the 2020NonCov group (Fig. S2). During the same period, the interval between ICU admission and mechanical ventilation increased during the 2 waves (Fig. S3).

### Device-related infection rates

#### Overall rate of HAI-ICU

The overall rate of HAI was higher in the 2020Cov group than in both the 2019Control and 2020NonCov groups. Among the patients

Data are shown as the number of patients n and percentage (%) or median and interquartile range (IQR). Between-group comparisons with significant p value set at 0.001. 2020Cov, SARS-CoV-2 COVID-19 group; 2020NonCov, non–COVID-19 group; ICU, intensive care unit; NS, not significant; SAPS II, Simplified Acute Physiological Score II.

#### Table 1

| Characteristic                                      | 2019Control (N = 39635) | 2020NonCov (N = 23798) | 2020Cov (N = 4465) | p     |
|-----------------------------------------------------|--------------------------|------------------------|-------------------|-------|
| Age (y), median (IQR)                               | 67.0 (56–75)             | 66.0 (55–74)           | 67.0 (58–74)      | NS    |
| Sex-ratio M/F                                       | 1.72                     | 1.84                   | 2.35              | <0.001<sup>a,b</sup>|
| Length of ICU stay (d), median (IQR)                | 6 (4–11)                 | 6 (4–11)               | 10 (6–19)         | <0.001<sup>a</sup>
| SAPS II, median (IQR)                               | 44 (32–58)               | 43 (32–57)             | 38 (30–49)        | <0.001<sup>b</sup>
| ICU case fatality, n (%)                            | 6498 (16.4)              | 3998 (16.8)            | 1017 (22.8)       | <0.001<sup>c</sup>
| Antibiotics ≥ 48 h around admission, n (%)          | 22 184 (56.1)            | 13 137 (55.3)          | 3098 (69.6)       | <0.001<sup>c</sup>
| Admission from, n (%)                               |                          |                        |                   |       |
| Home                                                | 21 784 (55.1)            | 13 809 (58.1)          | 1963 (44.0)       | <0.001<sup>a,b</sup>
| Nursing home                                        | 574 (1.5)                | 320 (1.3)              | 63 (1.4)          | NS    |
| Long-term care facility                             | 782 (1.8)                | 202 (0.9)              | 66 (1.5)          | NS    |
| Rehabilitation                                      | 626 (1.6)                | 305 (1.3)              | 42 (0.9)          | NS    |
| Other wards (acute care)                            | 14 201 (35.9)            | 7892 (33.2)            | 1973 (44.2)       | <0.001<sup>c</sup>
| Other ICU                                           | 1653 (4.2)               | 1225 (5.2)             | 352 (7.9)         | <0.001<sup>c</sup>
| Diagnostic category at admission, n (%)             |                          |                        |                   |       |
| Medical                                             | 26 886 (67.9)            | 16 627 (69.9)          | 4195 (94.1)       | <0.001<sup>a,b</sup>
| Emergency surgery                                   | 7160 (18.1)              | 4338 (18.2)            | 189 (4.2)         | <0.001<sup>c</sup>
| Scheduled surgery                                    | 5556 (14.0)              | 2809 (11.8)            | 75 (1.7)          | <0.001<sup>c</sup>
| Trauma, n (%)                                       | 2826 (7.2)               | 1817 (7.6)             | 155 (3.3)         | <0.001<sup>c</sup>
| Immunosuppression, n (%)                            | 5908 (15.3)              | 3345 (14.6)            | 625 (14.2)        | NS    |
| Including <500 Neutrophils/mm³, n (%)               | 652 (1.7)                | 360 (1.6)              | 48 (1.1)          | NS    |
| Device exposure, n (%)                              |                          |                        |                   |       |
| Intubation probe                                     | 24 109 (60.9)            | 15 131 (63.7)          | 2628 (58.9)       | <0.001<sup>a,b</sup>
| Central venous catheter                             | 26 706 (67.5)            | 17 089 (71.9)          | 2935 (65.8)       | <0.001<sup>a,b</sup>
| Urinary catheter                                    | 33 236 (86.0)            | 20 733 (88.1)          | 3353 (77.6)       | <0.001<sup>b</sup>
| Exposure duration (d), median (IQR)                 | 4 (2–10)                 | 5 (2–11)               | 12 (6–22)         | <0.001<sup>c</sup>
| Mechanical ventilation                              | 6 (4–12)                 | 7 (4–12)               | 12 (7–22)         | <0.001<sup>c</sup>
| Device utilization ratio, %                         | 50.9                     | 55.2                   | 64.0              | <0.001<sup>b</sup>
| Intubation probe                                     | 50.9                     | 55.2                   | 64.0              | <0.001<sup>b</sup>
| Central venous catheter                             | 68.5                     | 72.0                   | 72.4              | <0.001<sup>c</sup>

<sup>a</sup> Significant difference between 2020Cov and 2020NonCov.
<sup>b</sup> Significant difference between 2020NonCov and 2019Control.

Please cite this article as: Lepape A et al., Effect of SARS-CoV-2 infection and pandemic period on healthcare-associated infections acquired in intensive care units, Clinical Microbiology and Infection, https://doi.org/10.1016/j.cmi.2022.10.023
The proportion of change (%) was calculated as follows: \(\frac{\text{2020SIR} - \text{2019SIR}}{\text{2019SIR}} \times 100\%\). The number of predicted infections was obtained using regression models created from the 2019 data. The proportion of patients infected with an MDRB (all infections combined: pneumonia, BSI and CRB) was greater in both 2020 groups, except for non-fermenting Gram-negative bacilli that are more frequent in patients in the 2020Cov group (Table S4 and S5).

The proportion of patients carrying at least 1 targeted Microorganisms involved in HAI-ICU and antimicrobial resistance profile

The distribution of the different bacterial species of interest is different between the 2019Control and 2020NonCov groups. In 2020, only modest differences in bacterial ecology were found between the 2020Cov and 2020NonCov groups, except for non-fermenting Gram-negative bacilli that are more frequent in patients in the 2020Cov group (Table S4 and S5).

The proportion of patients infected with an MDRB (all infections combined: pneumonia, BSI and CRB) was greater in both 2020 groups (2020NonCov and 2020Cov) than in the 2019Control group. The proportion of patients infected with methicillin-resistant \textit{S. aureus}, carbapeneme-resistant enterobacteria, and CRPa was significantly greater in the 2020Cov group than in the 2020NonCov group (Table S5). It should be noted that all carbapeneme-resistant enterobacteria were isolated in VAP, but never in catheter associated bloodstream infection.

Discussion

The main result of the present study is that HAI-ICU, particularly VAP, were more frequent in both ICU populations during 2020 than in 2019, regardless of their COVID-19 status. This is because of extrinsic and intrinsic factors. Among the extrinsic factors, the pandemic had a major effect on the hospital and ICU organization [2]. The breakdown in infection prevention best practices is highly likely; however, it is probably variable among countries [12] and units. Moreover, it is not possible to further analyse the responsibilities of prevention practice in the present study because this is not recorded in our surveillance programme.

The higher rates of pneumonia and BSI have different determinants. VAP was at least 3 times more frequent in patients in the 2020Cov group than in the 2020NonCov group; such a high rate of VAP has been reported in several multicentre studies, for example

in the 2020NonCov group, the increase was partially because of more frequent VAP, but also, at a lesser extent, to more frequent BSI (including CRB) (Table 2).
and the historical 2019 Control cohorts, indicating that very old testing characteristics of the patients in the 2020Cov group. The surgical patients (i.e. corticosteroids and tocilizumab).

Moreover, we need to point out that nearly 15% of the patients with COVID-19 were not diagnosed with the use of PCR because of the lack of availability of this method at the beginning of the classical male predominance in patients with COVID-19 was found in the 2020Cov cohort [20]. Mortality was more frequent in the 2020Cov group despite a low severity score (Simplified Acute Physiological Score II) at admission; this could be explained by the early admission of patients in the 2020Cov group to ICU. Furthermore, there was a reduced direct admission to ICU, which is likely to be explained by a more frequent previous admission to a medical ward. Moreover, scheduled surgical activity was reduced in relation to reorientation of ICU beds towards COVID-19 in the European countries [2]. It is also important to note that antibiotic exposure measured around the ICU admission was very high in the 2020Cov group, approximately 70%. This has been well analysed in an editorial by De Waele et al. [21]: possible co-infections, use of immunomodulating medications, such as corticosteroids and interleukin inhibitors, and a longer duration of mechanical ventilation in patients in the 2020Cov group. As the understanding of COVID-19 progressed, the initial overexposure of patients with COVID-19 antibiotics for the fear of bacterial co-infection slightly decreased in our study (data not shown).

MDRB carriage was more frequent in patients in the 2020Cov group, especially among ESBL-producing enterobacterales and CRPa, a result possibly related to a high exposure to antibiotics at admission and during a previous stay in a ward. There was no remarkable difference in the distribution of the most frequent bacteria: enterobacterales were found at the same rate in all groups, and there was a slightly high rate of detection of infections resulting from P. aeruginosa in patients in the 2020Cov group. Furthermore, resistance levels were not very different: for instance, there was less ceftazidime resistance in Pseudomonas isolated from patients in the 2020Cov group, and only ESBL enterobacterales were slightly more frequently isolated from these patients. Taken together, these data suggest that the microbial epidemiology and resistance are not a major problem in SARS-CoV-2 infections.

Strengths and limitations

Surveillance network data from the REA-REZO are of value as a large number of patients are included, and because the network has existed for many years, the quality of the data is high. It also has the advantage of measuring the burden of HAI-ICU in the ICU population during the pandemic period, showing that patients in the 2020NonCov group were also concerned by the increase in HAI-IC. As the understanding of COVID-19 progressed, the initial overexposure of patients with COVID-19 antibiotics for the fear of bacterial co-infection slightly decreased in our study (data not shown).

MDRB carriage was more frequent in patients in the 2020Cov group, especially among ESBL-producing enterobacterales and CRPa, a result possibly related to a high exposure to antibiotics at admission and during a previous stay in a ward. There was no remarkable difference in the distribution of the most frequent bacteria: enterobacterales were found at the same rate in all groups, and there was a slightly high rate of detection of infections resulting from P. aeruginosa in patients in the 2020Cov group. Furthermore, resistance levels were not very different: for instance, there was less ceftazidime resistance in Pseudomonas isolated from patients in the 2020Cov group, and only ESBL enterobacterales were slightly more frequently isolated from these patients. Taken together, these data suggest that the microbial epidemiology and resistance are not a major problem in SARS-CoV-2 infections.

in 2 French cohorts, the rate of VAP was 43% [13] and 52% [14], and the main study on HAI-ICU in patients with COVID-19, conducted in Italy, reported a rate of 50% of VAP in intubated patients (26.0 [95% CI, 23.6–28.8] VAP per 1000 mechanical ventilation-days) [15]. In addition, during the 2 years of surveillance, no modification in the diagnostic practice of VAP were found in the different periods and groups (data not shown), and the high SIR of VAP corresponded to the 2 waves of the pandemic in France. The high rate of VAP in the 2020Cov was related to the lung tropism of SARs-CoV-2 and the super-infections, as shown, for instance, in a comparison between COVID-19 and in super-infections, as shown, for instance, in a comparison between COVID-19 and influenza [16]. Intrinsic factors related to the disease process itself included lung parenchymal damage, immune dysregulation, and an increased risk of thrombosis [17].

A High rate of BSI has also been reported elsewhere [18]. It is related to a more frequent intra-vascular device origin of infection, which could be attributed at least partially to the modification of the management of patients in the ICU [2]. In addition, it is also associated with a more frequent pulmonary origin (related to the more frequent VAP) and a decrease of digestive origin (fewer surgical patients) in patients in the 2020Cov group.

The surveillance data provide information about several interesting characteristics of the patients in the 2020Cov group. The median age of the 2020Cov cohort was similar to the 2020NonCov and the historical 2019Control cohorts, indicating that very old patients were not necessarily admitted to the ICU [19]. In addition,
pandemic. However, the risk of misclassifying these patients is limited by the strict recommendations from the ministry of health and learned medical societies for the case definition.

In conclusion, the data presented here indicate that HAI-ICU were more frequent during the COVID-19 period, whether the patients were admitted to ICU for COVID-19 or another cause. This implies that besides the specific role of COVID-19, particularly in pulmonary super-infection, the high in flow of patients decreases the quality of care provided to all patients, leading to an increased risk of HAI-ICU for all patients.

Author contributions
A.L., A.M., C.B., A.F., and A.S. designed the study. A.M. and C.V. analysed and interpreted the data. A.L. and A.M. wrote the manuscript. A.L., C.B., A.F., C.V., and A.S. revised the manuscript.

Transparency declaration
The authors declare that they have no conflicts of interest.

Acknowledgements
The authors are grateful to Philip Robinson for manuscript editing assistance.

The authors thank the members of the REA-REZO Network: Martin Maelle, Bourguilt Céline, Maxime Virginie, Lawrence Christine, Alvarez Antonio, Rohr Laetitia, Le Quoc Viet, Hayo François, Galliot Richard, Farfour Eric, Pugliesi Paul-Simon, Le Coq Muriel, Troche Gilles, Neuiler Caroline, Leblanc Pierre-Etienne, Ouzani Souad; Pilot Jérôme, Bordes-Couécou Stéphanie; Le Floc Anne-Sophie, Sechaud Dominique, Launoy Anne, Lavigne Thierry, Afandari Serge; Bulyez Stephanie; Belin Nicolas, Beilouny Bassam; Anne-Sophie, Sechaud Dominique; Launoy Anne, Lavigne Thierry; chowski Stanislas, Bernerd C; V Roques Adrien; Cayuela Marie-Anne; Cortes Esther, Fleurial Rossem Vanessa; Martin Audrey, Curnier Sylvie; Berrouba Aziz, Toro Alexandre; Pommier Christian, Haond Adrien, Canu Nathalie; Roche Anne-Claude, Galland Claude, Causse Robert; Bouillard Laurent, Munier-Marion Elodie; Florentin Arnaud; and Vincent Jean-François, Venot Christine.

Appendix A. Supplementary data
Supplementary data to this article can be found online at https://doi.org/10.1016/j.cmi.2022.10.023.

References
[1] Serafin RB, Póvoa P, Souza-Dantas V, Kalil AC, Salluh JF. Clinical course and outcomes of critically ill patients with COVID-19 infection: a systematic review. Clin Microbiol Infect 2021;27:47–54. https://doi.org/10.1016/j.cmi.2020.10.017.
[2] Aziz S, Abati YM, Alfazazi W, Evans L, Cirelli G, Fischkoff K, et al. Managing ICU surge during the COVID-19 crisis: rapid guidelines. Intensive Care Med 2020;46:1303–25. https://doi.org/10.1007/s00134-020-06092-5.
[3] Lakab I, Medam S, Ronfle R, Cassir N, Delamarre I, Hammad E, et al. Association between mortality and highly antimicrobial-resistant bacteria in intensive care unit-acquired pneumonia. Sci Rep 2021;11:16497. https://doi.org/10.1038/s41598-021-95852-4.
[4] Vacheron CH, Lepape A, Savey A, Machut A, Timsit JF, Vanhems P, et al. Increased incidence of ventilator-acquired pneumonia in coronavirus disease 2019 patients: a multicentric cohort study. Crit Care Med 2020;50:449–59. https://doi.org/10.1097/CCM.0000000000005297.
[5] Vacheron CH, Lepape A, Savey A, Machut A, Timsit JF, Comparot S, et al. Avoidable mortality of ventilator-associated pneumonia among patients with COVID-19. Am J Respir Crit Care Med 2022;206:161–9. https://doi.org/10.1164/rccm.202202-0357OC.
[6] Rea-Rezo. Surveillance et prévention des IAS en réanimation [Internet]. 2019 [cited 2019 September 4]. Available from: http://reaerrezo.chu-lyon.fr.
[7] Le Gall JR, Lemeshow S, Saulnier F. A new simplified Acute Physiology Score (SAPS II) based on a European/North American multicenter study. JAMA 1993;270:2957–63. https://doi.org/10.1001/jama.1993.03480590041.
[8] EUCAST. The European committee on antimicrobial susceptibility testing – EUCAST [Internet]. 2022 [cited 2022 January 21]. Available from: https://www.euusc.org.
[9] Plachouras D, Lepape A, Suetens C. EDCD definitions and methods for the surveillance of healthcare-associated infections in intensive care units. Intensive Care Med 2018;44:2216–8. https://doi.org/10.1007/s00134-018-1113-0.
[10] European Centre for Disease Prevention and Control (ECDC). Surveillance of healthcare-associated infections and prevention indicators in European intensive care units: HAI-Net ICU protocol, version 2.2. European Centre for Disease Prevention and Control and Prevention 2017 [Internet]. 2018 [cited 2018 January 23]. Available from: http://ecdc.europa.eu/en/publications-data/surveillance-healthcare-associated-infections-prevention-indicators-european.
[11] Weiner-Lusting LM, Pattabiraman V, Konnor RY, Patel PR, Wong E, Xu SY, et al. The impact of coronavirus disease 2019 (COVID-19) on healthcare-associated infections: an update and perspective. Infect Control Hosp Epidemiol 2022;43:12–25. https://doi.org/10.1017/ice.2021.362.
[12] Assi MA, Doll M, Pryor R, Cooper K, Bearman G, Stevens MP. Impact of coronavirus disease 2019 (COVID-19) on healthcare-associated infections: an update. Clin Microbiol Infect 2021;27:54. https://doi.org/10.1016/j.cmi.2020.10.017.
[13] Roger C, Collange O, Mezzarobba M, Abou-Arab O, Teule L, Garnier M, et al. French multicentre observational study on SARS-CoV-2 infections intensive care initial management: the French Corona study. Anaesth Crit Care Pain Med 2021;40:100931. https://doi.org/10.1016/j.accpm.2021.100931.
[14] Llitjos JF, Bredin S, Lascarrou JB, Soumagne T, Cojocaru M, Leclerc M, et al. Increased susceptibility to intensive care unit-acquired pneumonia in severe COVID-19 patients: a multicentre retrospective cohort study. Ann Intensive Care 2021;11:20. https://doi.org/10.1186/s13613-021-00812-w.
[15] Grasselli G, Scarcavilli V, Mangioni D, Scudeller L, Alagna L, Bartoletti M, et al. Hospital-acquired infections in critically ill patients with COVID-19. Chest 2021;160:454–65. https://doi.org/10.1016/j.chest.2021.04.002.
[16] de Marignan D, Vacheron CH, Ader J, Frobert E, Jaubert C, Le Coq A. A retrospective comparison of COVID-19 and seasonal influenza mortality and
outcomes in the ICUs of a French university hospital. Eur J Anaesthesiol 2022;39:427–35. https://doi.org/10.1097/EJA.0000000000001672.

[17] Boyd S, Nseir S, Rodriguez A, Martin-Loeches I. Ventilator-associated pneumonia in critically ill patients with COVID-19 infection: a narrative review. ERJ Open Res 2022;8:46–2022. https://doi.org/10.1183/23120541.00046-2022.

[18] Buetti N, Ruckly S, de Montmollin E, Reignier J, Terzi N, Cohen Y, et al. COVID-19 increased the risk of ICU-acquired bloodstream infections: a case-cohort study from the multicentric OUTCOMEREA network. Intensive Care Med 2021;47:180–7. https://doi.org/10.1007/s00134-021-06346-w.

[19] O’Driscoll M, Ribeiro dos Santos G, Wang L, Cummings DAT, Azman AS, Paireau J, et al. Age-specific mortality and immunity patterns of SARS-CoV-2. Nature 2021;590:140–5. https://doi.org/10.1038/s41586-020-2918-0.

[20] Pijls BG, Jolani S, Atherley A, Dercks RT, Dijkstra JIR, Franssen GHL, et al. Demographic risk factors for COVID-19 infection, severity, ICU admission and death: a meta-analysis of 59 studies. BMJ Open 2021;11:e044640. https://doi.org/10.1136/bmjopen-2020-044640.

[21] De Waele JJ, Derde L, Bassetti M. Antimicrobial stewardship in ICUs during the COVID-19 pandemic: back to the 90s? Intensive Care Med 2021;47:104–6. https://doi.org/10.1007/s00134-020-06278-x.