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### ▶ To cite this version:

Yassir Aarab, Theodore Debourdeau, Fanny Garnier, Mathieu Capdevila, Clément Monet, et al.. Management and outcomes of COVID-19 patients admitted in a newly created ICU and an expert ICU, a retrospective observational study. Anaesthesia Critical Care & Pain Medicine, 2024, 43 (1), pp.101321. 10.1016/j.accpm.2023.101321. hal-04281093

### HAL Id: hal-04281093 https://hal.science/hal-04281093v1

Submitted on 23 Jan2024

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# Management and outcomes of COVID-19 patients admitted in a newly created ICU and an expert ICU, a retrospective observational study

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#### **Keywords:**

COVID-19 AHRF Intensive care Mortality Surge capacity ICU outcomes

#### Abbreviations:

ACU, Acute Care Unit; AHRF, Acute Hypoxemic Respiratory Failure; ICU, Intensive Care Unit; LOS, Length of Stay; PACU, Post Anesthetic Care Unit; PIR, Patient to Intensivist Ratio; PNR, Patient to Nurse Ratio; SOFA, Sepsis-related Organ Failure Assessment.

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## A B S T R A C T

#### **Background:**

The COVID-19 pandemic abruptly increased the inflow of patients requiring intensive care units (ICU). French health institutions responded by a twofold capacity increase with temporary upgraded beds, supplemental beds in pre-existing ICUs, or newly created units (New-ICU). We aimed to compare outcomes according to admission in expert pre-existing ICUs or in New-ICU.

#### Methods:

This multicenter retrospective observational study was conducted in two 20-bed expert ICUs of a University Hospital (Expert-ICU) and in one 16-bed New-ICU in a private clinic managed respectively by 3 and 2 physicians during daytime and by one physician during the night shift. All consecutive adult patients with COVID-19-related acute hypoxemic respiratory failure admitted after centralized regional management by a dedicated crisis cell were included. The primary outcome was 180-day mortality. Propensity score matching and restricted cubic spline for predicted mortality over time were performed.

#### **Results:**

During the study period, 165 and 176 patients were enrolled in Expert-ICU and New-ICU respectively, 162 (98%) and 157 (89%) patients were analyzed. The unadjusted 180-day mortality was 30.8% in Expert-ICU and 28.7% in New-ICU, (log-rank test, p = 0.7). After propensity score matching, 123 pairs (76 and 78%) of patients were matched, with no significant difference in mortality (32% vs. 32%, OR 1.00 [0.89; 1.12], p = 1). Adjusted predicted mortality decreased over time (p < 0.01) in both Expert-ICU and New-ICU.

### **Conclusions:**

In COVID-19 patients with acute hypoxemic respiratory failure, hospitalization in a new ICU was not associated with mortality at day 180.

### **1. Introduction**

The COVID-19 pandemic has led to an unprecedented outbreak of acute hypoxemic respiratory failure (AHRF) requiring Intensive Care Unit (ICU) admission for respiratory support [1,2]. Recent surveys have reported a 24–42% mortality rate [3–7]. While many studies have focused on predictors of hospital mortality, only a few have assessed the factors related to surge capacity organization [8–11]. Healthcare systems worldwide have expanded ICU capacities, either by converting exhibition centers into ICUs, or by expanding ICUs in operating rooms, Post Anesthetic Care Units (PACU), and other wards [12,13]. In France, 5531 ICU beds were available before the outbreak. Within the two first months of the pandemic, 4806 new ICU beds were created, a 95% increase. These new ICU beds were created by upgrading Acute Care Units (ACU, 2283 beds, 47.5%), PACU and operating rooms (1522 beds, 31.6%), other conventional units (374 beds, 7.8%) or by the actual build-up of new ICU beds (627 beds, 13%). Among these, 43 institutions were authorized to create new ICUs accounting for 399 beds [14].

Observational studies around the world have identified an association between higher COVID-19 patient mortality and newly created or temporary ICU beds [8,9]. Conversely, an international study reported that admission to a surge capacity beds unit was not associated with increased mortality [11].

To our knowledge, a comparison between expert ICUs in University Teaching Hospital (Expert-ICU) and newly created but qualitatively comparable ICUs in a private clinic (New-ICU) has not been previously described in France. We aim to compare outcomes among critically ill patients admitted for COVID-19 AHRF in Expert-ICU and New-ICU.

### 2. Methods

#### 2.1. Study design and population

We conducted a retrospective analysis of prospectively collected data from two expert ICUs at the Montpellier Teaching University Hospital and one newly created ICU at a Montpellier private clinic.

From March 2020 to February 2022, all consecutive adult patients admitted to participating ICUs with confirmed COVID-19 infection and related AHRF as commonly defined were included [15]. Exclusion criteria were non-COVID-related AHRF, intubation for neurologic impairment, do-not-intubate order, and the patient's decision not to participate. The population was sub-divided into two groups according to the ICU of admission: the "Expert-ICU" group when admitted to one of the two expert university ICUs and the "New-ICU" group when admitted to the newly created non-academic ICU. Institutional ethical approval was obtained (IRB n8 IORG0010765 – CER-2022-YA01). The need for written consent was waived in accordance with French Law. Patients and/or their next of kin were informed (oral and written). We followed the STROBE guidelines for observational studies [16].

#### 2.2. Clinical management and ICU organization

Medical decisions such as the indication for intubation, the use of respiratory support devices, and treatments were left to the discretion of the attending physician. All physicians in the ICUs were affiliated with the French Society of Anesthesia and Critical Care and/or the French Intensive Care Society and followed the national and international guidelines for critically ill and COVID-19 patients' management [17–20].

Expert-ICU physicians were all critical care anesthesiologists who had been working in their unit for several years (from 3 to 31 years). One unit was a 20-bed medical/surgical ICU and tertiary trauma center, and the other was a 20-bed medical/surgical ICU and liver transplantation center. Both units have been in existence for over 50 years. There were also residents ranging from the 1st and the 4th year (one resident for every 4 patients, supervised by a physician for every 6–8 patients). Night shifts were covered by two residents and two senior physicians.

New-ICU physicians were intensivists trained either in anesthesiology and intensive care or in medical intensive care. They had between 3–5 years of experience in other ICUs at tertiary care hospitals and were recruited in 2020 by the private clinic to build up the New-ICU. The New-ICU was a 16-bed unit divided into 8 ICU beds and 8 ACU beds which were upgraded into a 16-bed ICU at the peak of the COVID-19 pandemic. Two physicians were in charge of 16 patients during daytime: two senior physicians or a senior physician with a resident with an ordinal replacement license (4th or 5th year of specialization in intensive care). Night shifts were covered by either one replacement resident or by one senior physician for the 16 beds.

On March 26th, 2020, the Clinique Saint Jean Sud de France (private clinic) initially received emergency authorization to open critical care beds in the new ICU for a 4-month period. This period corresponds to the first wave in France, which had relatively spared the South of France. This allowed the New-ICU to recruit their intensivists, to progressively acquire all the necessary equipment for the management of critically ill patients (advanced intensive care ventilators, dialysis generator, extracorporeal life support machine), and above all to organize theoretical and practical training for all the non-medical staff of the newly created department. This training was organized by the local intensivists, with two mandatory training cycles based on intensive care nurse programs from French national scientific societies and procedural simulation of life-threatening situations. The implementation of the unit followed the national and international guidelines issued during the crisis [17,21]. Subsequently, on September 26th, 2020, at the beginning of the second wave in France, a new temporary authorization was granted for ICU activity for a six-month period with successive renewals, which are still ongoing. Taking into account the young age of the unit and its staff, the patient-to-nurse ratio (PNR) was always maintained between 1:2 and 1:2.5, regardless of the number of critically ill patients or mechanically ventilated COVID-19 or non-COVID-19 patients. The patient-to-intensivist ratio (PIR) was left to the discretion of the medical team, depending on their local capabilities and what the crisis situation permitted.

#### 2.3. Data collection

All clinical variables were recorded prospectively from ICU admission until death or hospital discharge. A phone call to the patient or next of kin, or querying the national register of deaths enabled us to complete the follow-up for six-month outcomes. Collected data included demographic characteristics, comorbidities, severity scores at admission, clinical management, and ICU-related events. We defined the "At least one major comorbidity" variable as previously reported [22].

### 2.4. Outcomes

The primary outcome was the 180-day mortality. The second-ary outcomes were 28-day, 90day, and ICU mortality, ICU and in-hospital length of stay (LOS), rate of intubation, duration of invasive mechanical ventilation, the use of organ support, and ICU-related events.

#### 2.5. Statistical analysis

For continuous data, the Gaussian distribution was checked using Shapiro-Wilk or Kolmogorov-Smirnov tests. Data were described as either median [interquartile range] or mean [standard deviation (SD)] or number (percentage). Fisher test, chi-square test, analysis of variance, and Wilcoxon–Mann–Witney test were used to compare variables as appropriate.

Two propensity score analyses (main and secondary) were used to reduce selection bias, estimated by fitting a logistic regression with the following variables: 1/ for the main propensity score = Sepsis-related Organ Failure Assessment (SOFA), comorbidities and endotracheal intubation in ICU; 2/ for the secondary propensity score = SOFA, comorbidities, endotracheal intubation, Dexamethasone, Tocilizumab, convalescent plasma and antibiotics at admission. Each patient in New-ICU group was matched with a patient in Expert-ICU group with the closest estimated propensity score within a specified range ( \_0.10 of the pooled standard deviation of estimated propensity scores).

First, univariate analyses were performed to compare characteristics and outcomes between groups before and after propensity score matching.

Second, mortality rates were calculated among patients managed in both Expert-ICU and New-ICU groups. Then, Kaplan–Meier curves with log-rank tests were computed to compare the cumulative incidence of 180-day mortality between groups. We also estimated hazard ratios for dying within 180 days from admission between Expert-ICU and New-ICU groups using a Cox regression model after adjustment for age, gender, SOFA score, and comorbidities.

Third, factors associated with 180-day mortality were analyzed using a multivariate logistic regression model with mortality as the dependent variable. Statistically significant variables with p < 0.20 on univariate analysis were introduced as predictive factors to the complete model.

Fourth, to assess the evolution of mortality over time, the cohort was divided into 8 time period of 3 months each. Restricted cubic splines were used to assess the evolution of 180-day mortality over time, adjusted on age, gender, SOFA score, and comorbidities. A three-way ANOVA test was performed to assess the interaction between time and ICU on the adjusted 180-day mortality.

A p-value of </= 0.05 was considered statistically significant. All statistical analysis were conducted using R statistical software version 4.2.2 (R Foundation for Statistical Computing, Vienna, Austria).

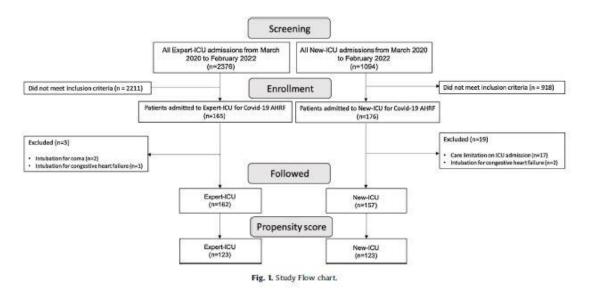


Table 1

Baseline characteristics of the studied population and comparison between patients managed in Expert-KU and New-KU after main propensity score matching,

Baseline characteristics	Expert-ICU (n = 123)	New-ICU (n = 123)	p value
Age, years, mean (SD)	65(11)	64(13)	0.64
Male gender, n(%)	85 (69)	82 (67)	0.78
BMI, Kg/m <sup>2</sup> , mean (SD)	30 (13)	29(5)	0.42
SOFA, median (IQR)	6 (3-11)	6(3-11)	0.77
SAPS II	41 (17)	45 (20)	0.13
Comorbidities, n (%)			
Hypertension	59 (48)	64(52)	0.34
Chronic heart failure	17 (14)	20(16)	0.60
Chronic obstructive pulmonary disease	13 (11)	12(10)	0.45
Diabetes mellitus	36 (29)	35(28)	0.15
Cancer	14(11)	15(12)	0.49
Chronic kidney disease	15 (12)	11 (9)	0.53
Chronic kidney dialysis	5 (4)	5(4)	1.00
Obstructive sleep apnea syndrome	16 (13)	13(11)	0.87
Cirrhosis	9(7)	2(2)	0.05
Immunodeficiency	11 (9)	9(7)	0.80
Solid organ transplantation	6 (5)	2(2)	0.28
Current smoking status	8 (7)	9 (7.0)	0.90
At least 1 major comorbidity*	43 (35)	42 (34)	0.47

BMI, Body mass index; ICU, Intensive Care Unit; IQR, Interquartile range; SAPS II, Simplified Acute Physiology Score; SD, Standard deviation; SOFA, Sepsis-related Organ Failure Assessment, \* At least one major comorbidity includes chronic respiratory diseases; chronic heart disease; solid tumors; liver cirrhosis; immunodeficiency induced by drugs; hematological malignancies.

### 3. Results

#### **3.1. Study population**

Over the two-year study period, 165 patients with confirmed COVID-19 AHRF were admitted to Expert-ICU and 176 were admitted to New-ICU. After the exclusion of 3 and 19 patients respectively, primarily due to care limitations on admission in the ICU, 162 (98%) and 157 (90%) patients were analyzed respectively (Fig. 1). Demographic data and clinical characteristics are reported in Table A1. The main differences between both Expert-ICU and New-ICU groups were age (61.3 [12.6] vs. 65.5 [12.3], p < 0.01), gender (Male: 98 (60.4%) vs. 114 (72.6%), p = 0.03), and history of cirrhosis (12 (7.4%) vs. 2 (1.3%), p = 0.02) respectively (Table A1).

After propensity score matching, 123 matched pairs of patients (76 and 78%) respectively were generated and no variable differed significantly between groups (Table 1). After secondary propensity score matching, 104 matched pairs of patients (64 and 66%) respectively were generated and no variable differed significantly between groups (Table A.4).

#### 3.2. Mortality and associated risk factors

No significant difference was observed in the unadjusted 180- day mortality between the patients in the Expert-ICU and in the New-ICU groups (50 (30.8%)) vs. 45 (28.7%, log-rank test, p = 0.7) (Fig. 2). No significant difference was found for 28-day mortality before and after main and secondary propensity scores matching (Table A.2, A.3 and A.5), neither for 90-day mortality before and after propensity scores matching (Table A.2, A.3 and A.5). After control for potential confounders in an adjusted Cox model, admission in New-ICU was not associated with higher mortality (Hazard Ratio 0.75 [0.49–1.13]; p = 0.2). In a multivariate analysis by logistic regression, there was no significant difference in 180- day mortality between New-ICU and Expert-ICU (OR 0.57 [0.31– 1.02]; p = 0.07). Independent factors associated with mortality in multivariate logistic regression are reported in Table 2.

The adjusted relation between the periods of admission and predicted 180-day mortality is reported in Fig. 3. There was a significant difference in adjusted predicted day-180 mortality in both groups over time, (p < 0.001 and p < 0.01 respectively for Expert-ICU and New-ICU). In a three-way ANOVA test, there was no significant interaction between time and ICU (p = 0.44), and no significant ICU effect was found (p = 0.81), while adjusted predicted mortality decreased over time (p = 0.04). Figure A.1 reports the unadjusted relation between the period of admission and predicted day-180 mortality in both groups, with no significant difference between New-ICU and Expert-ICU.

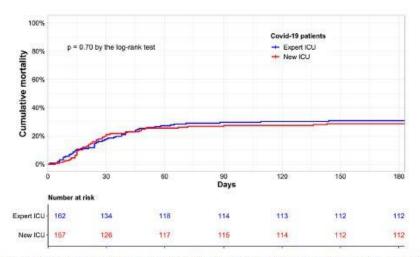


Fig. 2. Kaplan-Meier curves for 180-day mortality in Expert-ICU and New-ICU. Cumulative incidence of mortality according to the area of hospitalization. The unadjusted cumulative 180-day mortality (Y-axis) is represented according to days since ICU admission until day 180 (X-axis). Using Kaplan Meier curves with log rank tests, no significant difference was observed in the unadjusted cumulative 180-day between the patients in the Expert-ICU (blue) and in the New-ICU (red) groups (50 (30.8%) vs. 45 (28.7%); log-rank test, p = 0.7)

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Factors associated with 180-day mortality with adjusted Cox model and multivariate analysis.

Adjusted Cox model	Hazard rati	io 95% CI	p value	
New-ICU	0.75	0.49-1.13	0,2	
Age (per year)	1.08	1.05-1.10	< 0.01	
Gender (male)	1.85	1.15-2.97	0.01	
SOFA score	1.10	1.05-1.15	< 0.01	
At least 1 major comorbidity <sup>a</sup>	1.49	0.98-2.25	0.06	
Multivariate analysis	ß coefficient	Odd Ratio (95% CI)	p value	
New-ICU	-0.5621	0.57 [0.31-1.02]	0.07	
Age (per year)	0.0815	1.08 [1.05-1.12]	< 0.01	
Gender (male)	0.5740	1.78 [0.95-3.39]	0.08	
SOFA score	1.2062	3.34 [1.87-6.12]	< 0.01	
At least 1 major comorbidity <sup>a</sup>	0.8792	2.41 [0.51-10.26]	0.24	

ICU, Intensive care unit; SOFA, Sepsis-related Organ Failure Assessment.

<sup>a</sup> At least one major comorbidity includes chronic respiratory diseases; chronic heart disease; solid tumors; liver cirrhosis; immunodeficiency induced by drugs; hematological malignancies.

#### 3.3. Clinical management

When the overall population was compared, there were significant differences in dexamethasone and antibiotic use, ventilator management, other organ supports use, ICU LOS and hospital LOS between groups (Table A.2). However, after main and secondary propensity scores matching no difference remained except for extracorporeal life support use (p = 0.01) (Table A.3 and A.5).

Note that, the PNR was 2.7 (40:15) in Expert-ICU group and 2.3 (16:7) in New-ICU group). The PIR was 6.7 (40:6) vs. 8 (16:2) respectively.

### 4. Discussion

#### 4.1. Main result

No significant difference was observed in 180-day mortality between the COVID-19 patients admitted into a newly created but permanent ICU in a private clinic (New-ICU group) and expert ICUs at a Teaching University Hospital (Expert-ICU group) during the second, third, and fourth waves in France. There was a significant decrease in adjusted predicted mortality over time in both groups.

#### 4.2. French and regional response during the COVID-19 outbreak

To prevent ICUs from being overwhelmed, the French healthcare system created almost 5,000 additional ICU beds, either by upgrading ACU, PACU, and operating rooms or by creating new beds in institutions that may or may not have had an ICU prior to the outbreak [14]. The distribution of these new beds could be variable and adapted to organizational specificities in each region [23–25]. This adaptability was possible thanks to (1) the versatility of the physicians trained in intensive care, regardless of their usual workplace (ICUs, operating rooms and anesthesia care, emergency departments); (2) the legal frame surrounding intensive care practices (unit architecture, nurse staffing, and medical coverage), and (3) the freely accessible updated national guidelines [26]. In our region, a crisis cell coordinated by the regional health agency and the Montpellier Teaching University Hospital brought together all health institutions and their physicians trained in intensive care in order to organize the creation of ICU beds according to each institution's capacity.

#### 4.3. Staff experience and training

Lower in-hospital mortality has been reported for COVID-19 patients admitted to university hospitals (28.2%) when compared to other ICUs (general: 36.4% - general with university characteristics: 41.2% - p = 0.003) [8]. This may be correlated with less experienced staff, which has been associated with higher mortality in temporary ICU [9]. Indeed, newly created ICU beds are often managed by nurses with little or no experience in intensive care (from operating rooms and conventional wards), and sometimes by less experienced physicians (residents, physicians usually working exclusively in anesthesiology or emergency departments).

In our study, the New-ICU had intensivists in charge with at least 3 years of experience as senior physicians in a university hospital. When night shifts were covered by a resident, they were supervised by a senior physician on call. The nurses had no previous experience in ICUs but primarily worked in ACUs, and received 4 months (1st surge) of intensive theoretical and practical training as described above. Moreover, the trained staff was maintained between surges even with lower patient inflow. These non-peak periods were put to good use either by repeating the previous training courses or by implementing novel mandatory cycles of

training, again with theoretical and practical training using procedural simulation. This continuous training became an integral part of the unit's organization in order to offset the lack of intensive care experience. We can speculate that this continuous training may partially explain the similar mortality rates between Expert-ICU and New-ICU in our study and the comparable reduction in adjusted mortality rate over time. For example, Schellenberg et al. reported that surge ICUs did not display lower rates of early mobilization thanks to the training and educational efforts of surge ICU managers [27].

#### 4.4. Staff resources and workload

The association between staff resources and patient outcomes has been reported in contexts other than the COVID-19 surge [28–30]. During the COVID-19 surge, higher mortality has been associated with high ICU admission overflow and with newly created ICU beds or temporary ICUs when PNR was 13:1 vs. 4:1 and PIR was 10:1 vs. 6:1 respectively [8,9]. In contrast, in the present study, PNR in Expert-ICU and New-ICU was 2.7 (20:8 and 20:7) and 2.3 (16:7) respectively, and PIR was 6.7 (20:3) and 8 (16:2) respectively.

There is no recommended PIR ratio in France, but previously reported optimal PIR in a large retrospective cohort was 7.8, with a significant increase in ICU and hospital mortality both above and below this ratio [30].

According to the French framework for ICU organization, both Expert-ICU and New-ICU in our study worked to always maintain the recommended PNR of 2.5 patients per nurse. The centralized regional management for ICU admissions by the crisis cell prevented sudden and unexpected ICU overflow. Locally, institutions decided to cancel elective surgeries and redeploy nurses and anesthesia nurses from operating rooms and wards. This likely explains the discrepancy between our study and other reports. Indeed, similar mortality rates between conventional ICUs and operating room ICUs or other surge capacity beds have been reported [10,11]. The key factors were lower workload as estimated by PNR, nurse training level, and the longer duration of this high workload which was linked to the duration of the epidemic wave. Additionally, this organization likely helped to avoid the long-lasting psychological impact reported among care providers during the COVID-19 pandemic [31].

The global UNITE-COVID study, an international point prevalence study among 4994 COVID-19 patients from 280 ICUs, did not find a difference in mortality according to admission to a surge capacity beds unit or conventional ICU beds. They applied a limited increase in PNR from 2 to 2.5 [11]. Most of their centers were teaching hospitals and the authors concluded to a limited applicability of their results. Thus, the present study confirms and extends the applicability of an adaptive resources and patient allocation strategy between expert units in teaching hospitals and smaller centers nearby to optimize patient management. We also reported a comparable incidence of hospital-acquired pneumonia of 43% in Expert-ICU and 45% in New-ICU (Table A3), which is similar to the incidence described in a recent international study on 3388 severe COVID-19 patients (45%) [3].

#### 4.5. What we have learned for future crisis

A few years earlier, lessons from terrorist attacks in Paris led to the creation of a Damage Control for Terrorist Attack Victims program [32]. The COVID-19 surge reminded us that ICUs and their staff must always be prepared for a massive influx of patients from unusual events by having: procedures for triage, designation and certification of trauma centers or new ICUs to implement critical care networks, data collection with registries, and specific continuous training [33]. A pre-planned rapid response to ICU bed requirements is crucial, but a higher and permanent number of ICU beds is mandatory. These beds could be allocated between expert centers in teaching hospitals, and smaller centers (regional hospitals and private clinics) to avoid ICU overflow and high workload, if the mandatory quality of care conditions mentioned above are met. The management of critically ill COVID-19 patients in ICU surge capacity beds is feasible with a good quality of care when conditions of safety (caregiver to patient ratio) and training are fulfilled. Another condition would be to avoid the ICU overflow within a unit or an institution as much as possible, arguing for the construction of new ICUs in institutions that are not endowed.

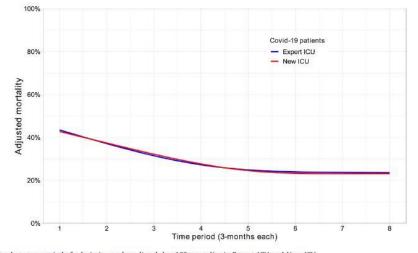


Fig. 3. Adjusted relation between period of admission and predicted day-180 mortality in Expert-ICU and New-ICU. The predicted day-180 mortality (Y-axis) after adjustment on SOFA score, age and gender, is represented according to the 8 time periods of 3 months each (x-axis) for Expert-ICU (blue) and New-ICU, red). Using a restricted cubic spline model for time periods, there was a significant difference in adjusted predicted day-180 mortality in both groups, (p < 0.001 and p < 0.01 respectively for Expert-ICU and New-ICU).

#### 4.6. Limitations

First, despite similar admission severity scores between groups (which rule out major differences in patient severity), there may still be an undetected imbalance between groups. Main confounders were addressed through propensity score matching, but the risk of unmeasured confounders still exists. For example, the Expert-ICU group had a higher number of cirrhotic patients because of the liver transplantation center. Anyway, cirrhosis was not identified as an independent risk factor for mortality.

Second, patients managed in Expert-ICU more frequently required extracorporeal life support (either extracorporeal mem-brane oxygenation or high flow extracorporeal carbon dioxide removal). However, there were no differences in other organ supports including duration of invasive mechanical ventilation and mortality in propensity scores matched groups.

Third, we excluded 17 patients with a collegiate "do not intubate" order in the New-ICU group. This ethical decision is usually made at the emergency department after medical examination by both an emergency physician and an intensivist. Those patients were not proposed to Expert-ICU, in line with our regional strategy to relieve our tertiary care centers. The decisions were always reassessed at New-ICU admission after in-depth interviews with family and the attending physician and were revised if appropriate [34].

Finally, the retrospective design of the study along with its small sample size and the limited external validity beyond France limits the strength of our conclusions. Nonetheless, it's worth noting that we had no missing data, and our clinical outcomes, such as mortality rates, are consistent with other international reports [7,8].

### **5.** Conclusion

No significant difference was observed in the unadjusted 180- day mortality, other outcomes or clinical management between the COVID-19 patients admitted in the Expert-ICU and New-ICU groups. Our results suggest the feasibility of providing safe and effective care for COVID-19 patients when the workload is evenly distributed and staff training is adequately maintained in a New- ICU. This approach could potentially reduce the usual workload for medical and non-medical staff and offer comparable high-quality care in case of a massive inflow of patients without overwhelming expert centers.

### Authors' contributions

SJ designed the study, participated in manuscript editing, and approved its final version. ADJ participated in manuscript editing, and approved its final version. YA and TD, contributed to conceptualization and design of the protocol, analyzed data and wrote the first draft of this submission. JP performed the statistical analysis and participated in manuscript editing. FG, MC, CM, GD, JC and XC revised the report critically for important intellectual content and approved the final version of the manuscript.

#### **Research ethics approval**

Institutional ethical approval was obtained (IRB n8 IORG0010765 – CER-2022-YA01). The need for written consent was waived according to the French Law

### Funding

This study has not been funded by any external source.

#### **Data sharing statement**

The data analyzed and presented in this study are available from the corresponding author on reasonable request, providing the request meets local ethical and research governance criteria after publication. Patient-level data will be anonymized and study documents will be redacted to protect the privacy of trial participants.

#### Human and animal rights

The authors declare that the work described has been carried out in accordance with the Declaration of Helsinki of the World Medical Association revised in 2013 for experiments involving humans as well as in accordance with the EU Directive 2010/63/EU for animal experiments.

#### Informed consent and patient details

The authors declare that this report does not contain any personal information that could lead to the identification of the patient(s).

#### **Conflict of interest**

SJ reports receiving consulting fees from Drager, Medtronic, Mindray, Fresenius, Baxter, and Fisher & Paykel. ADJ reports receiving remuneration for presentations from Medtronic, Drager and Fisher & Paykel. All other authors declare no competing interests.

#### Acknowledgments

The authors gratefully acknowledge all the clinical research centers, and patients involved in the study, without whom we would not have been able to perform this work.

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