

Contemporary assessment of short- and functional 90-days outcome in old intensive care patients suffering from COVID-19

Raphael Romano Bruno, Bernhard Wernly, Antonio Artigas, Kristina Fuest, Stefan J. Schaller, Lisa Dannenberg, Detlef Kindgen-Milles, Malte Kelm, Michael Beil, Sigal Sviri, Muhammed Elhadi, Michael Joannidis, Sandra Oeyen, Eumorfia Kondili, Rui Moreno, Susannah Leaver, Bertrand Guidet, Dylan W. De Lange, Hans Flaatten, Wojciech Szczeklik, Christian Jung

Article - Version of Record

Suggested Citation:

Bruno, R. R., Wernly, B., Artigas, A., Fuest, K., Schaller, S. J., Dannenberg, L., Kindgen-Milles, D., Kelm, M., Beil, M., Sviri, S., Elhadi, M., Joannidis, M., Oeyen, S., Kondili, E., Moreno, R., Leaver, S., Guidet, B., De Lange, D. W., Flaatten, H., ... Jung, C. (2024). Contemporary assessment of short- and functional 90-days outcome in old intensive care patients suffering from COVID-19. Journal of Critical Care, 86, Article 154984. https://doi.org/10.1016/j.jcrc.2024.154984

Wissen, wo das Wissen ist.



This version is available at:

URN: https://nbn-resolving.org/urn:nbn:de:hbz:061-20250507-113530-0

Terms of Use:

This work is licensed under the Creative Commons Attribution 4.0 International License.

For more information see: https://creativecommons.org/licenses/by/4.0



Contents lists available at ScienceDirect

Journal of Critical Care



journal homepage: www.journals.elsevier.com/journal-of-critical-care

Contemporary assessment of short- and functional 90-days outcome in old intensive care patients suffering from COVID-19

Raphael Romano Bruno^{a,1}, Bernhard Wernly^{b,c,1}, Antonio Artigas^d, Kristina Fuest^e, Stefan J. Schaller^{f,g}, Lisa Dannenberg^a, Detlef Kindgen-Milles^h, Malte Kelm^{a,i,j}, Michael Beil^k, Sigal Sviri^k, Muhammed Elhadi¹, Michael Joannidis^m, Sandra Oeyenⁿ, Eumorfia Kondili^o, Rui Moreno^{p,q}, Susannah Leaver^r, Bertrand Guidet^{s,t}, Dylan W. De Lange^u, Hans Flaatten^v, Wojciech Szczeklik^w, Christian Jung^{a,i,j,*}, COVIP study group and collaborators on behalf of the COVIP study group²

^b Department of Internal Medicine, General Hospital Oberndorf, Teaching Hospital of the Paracelsus Medical University, Salzburg, Austria

^c Institute of General Practice, Family Medicine and Preventive Medicine, Paracelsus Medical University of Salzburg, Salzburg, Austria

e Technical University of Munich, School of Medicine and Health, Department of Anesthesiology and Intensive Care Medicine, Munich, Germany

- ^f Medical University of Vienna, Department of Anaesthesia, Intensive Care Medicine and Pain Medicine, Division of General Anaesthesia and Intensive Care Medicine, Vienna, Austria
- ^g Charité Universitätsmedizin Berlin, Corporate Member of Freie Universität Berlin and Humboldt-Universität zu Berlin, Department of Anesthesiology and Intensive Care Medicine (CCM/CVK), Berlin, Germany
- ^h Department of Anesthesiology, Heinrich Heine University, Dusseldorf, Germany
- ⁱ Heinrich-Heine University, Medical Faculty, Department of Cardiology, Pulmonology and Vascular Medicine, Düsseldorf, Germany
- ^j CARID (Cardiovascular Research Institute Düsseldorf), Düsseldorf, Germany
- ^k Dept. of Medical Intensive Care, Hadassah Medical Center and Faculty of Medicine, Hebrew University of Jerusalem, Israel
- ¹ Faculty of Medicine, University of Tripoli, Tripoli, Libya
- m Division of Intensive Care and Emergency Medicine, Department of Internal Medicine, Medical University Innsbruck, Innsbruck, Austria
- ⁿ Department of Intensive Care 1K12IC, Ghent University Hospital, Ghent, Belgium
- ^o Department of Intensive Care Medicine, Intensive Care Unit, University Hospital of Heraklion, Greece
- ^p Hospital de São José, Unidade Local de Saúde São José, Centro Clinico Académico de Lisboa (CCAL), Lisboa, Portugal
- ^q Faculdade de Ciências da Saúde, Uniuversidade da Beira Interior, Covilhã, Portugal
- r General Intensive Care, St George's University Hospitals NHS Foundation Trust, London, United Kingdom
- ⁸ Sorbonne Universités, UPMC Univ Paris 06, INSERM, UMR_S 1136, Institut Pierre Louis d'Epidémiologie et de Santé Publique, Equipe: Épidémiologie Hospitalière
- Qualité et Organisation Des Soins, F-75012 Paris, France

^t Assistance Publique - Hôpitaux de Paris, Hôpital Saint-Antoine, Service de Réanimation Médicale, Paris F-75012, France

^u Department of Intensive Care Medicine, University Medical Center, University Utrecht, the Netherlands

- v Department of Clinical Medicine, University of Bergen, Department of Research and Development, Haukeland University Hospital, Bergen, Norway
- w Jagiellonian University Medical College, Center for Intensive Care and Perioperative Medicine, Krakow, Poland

ARTICLE INFO	A B S T R A C T
Keywords:	Purpose: There are limited data about the outcome of old intensive care (ICU) patients suffering from Covid-19 in
Covid-19 Elderly	the post-vaccination era. This study distinguishes the pre- and post-acute illness living conditions of ICU sur- vivors from non-survivors
Long-term outcomes COVIP-study	<i>Methods</i> : This prospective international multicenter study included 642 old (\geq 70 years) ICU patients, including data ranging from pre-illness condition to functional 90 days follow-up. The primary endpoint was the difference

* Corresponding author at: Division of Cardiology, Pulmonology, and Vascular Medicine, University Duesseldorf, Moorenstraße 5, 40225 Duesseldorf, Germany. *E-mail addresses:* christian.jung@med.uni-duesseldorf.de (C. Jung), covip@med.uni-duesseldorf.de (COVIP study group and collaborators on behalf of the COVIP study group).

study group).

¹ Contributed equally.

 $^{2}\,$ COVIP-study group (see Supplement 1).

https://doi.org/10.1016/j.jcrc.2024.154984

Received 21 March 2024; Accepted 21 November 2024

Available online 3 December 2024

0883-9441/© 2024 The Author(s). Published by Elsevier Inc. This is an open access article under the CC BY license (http://creativecommons.org/licenses/by/4.0/).

^a Heinrich-Heine-University Duesseldorf, Medical Faculty, Department of Cardiology, Pulmonology and Vascular Medicine, Duesseldorf, Germany

^d Department of Intensive Care Medicine, CIBER Enfermedades Respiratorias, Corporacion Sanitaria Universitaria Parc Tauli, Autonomous University of Barcelona, Sabadell, Spain

of living conditions of ICU-survivors before ICU admission and 90-days after ICU discharge. Secondary outcomes were 90-days mortality, and quality of life.

Results: A total of 642 patients were included. Significantly more ICU survivors lived at their own homes without support before ICU admission than non-survivors (p = 0.016), while more non-survivors resided in nursing homes (p = 0.016). ICU mortality was 39 %, 30-days and 90 days mortality were 47 % and 55 %. After 90 days, only 22 % maintained the same living conditions. Surviving patients viewed ICU admission positively after 90 days, while relatives were more uncertain. Quality of life indicated a self-reported average score of 60 (50–75). *Conclusion:* Living conditions influence the outcome of critically ill old patients suffering from Covid-19. Only a minority returned to their initial habitat after ICU survival.

Trial registration number NCT04321265

1. Introduction

Despite mass vaccination campaigns against severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), infections with patients suffering from the associated coronavirus disease 2019 (COVID-19) are being continuously observed (1). In this "post-vaccination era", chronological age is still one of the dominant risk factors for poor outcomes in older patients suffering from infections despite a sufficient vaccination tentative (2). Older individuals aged 70 years and above are particularly vulnerable to severe complications, often necessitating admission to the intensive care unit (ICU) (3). Mortality rates in this population account for up to 50 % (4-6). Managing critically ill old patients with COVID-19 poses challenges to the ICU and healthcare systems. Thus, understanding additional factors outside age influencing outcomes, including pre-ICU functional status such as symptoms of frailty and post-ICU functional outcomes, is paramount for optimizing management (7). In this context, understanding the pre-ICU conditions of older patients suffering from acute COVID-19 is crucial for comprehending the baseline health status that contributes to the complexity of their critical illness. Numerous factors might influence the outcome, ranging from co-existing conditions like frailty (8,9), cardiovascular diseases (10), diabetes (11), and respiratory conditions to the overall functional status (12) and cognitive ability (11,13). During ICU treatment, these pre-ICU conditions might influence decisions about withholding or withdrawing life-sustaining therapy (14,15), organ support (16,17), and subsequent outcomes. Beyond the acute phase of intensive care, the long-term functional outcomes of older COVID-19 patients post-ICU discharge represent a critical aspect of their overall recovery (18). There is very little evidence about functional outcomes after ICU treatment including the quality of life and the individual living conditions that considers different endpoints rather than just survival.

The present study prospective critical care study follows individual patients through the complete trajectory before, during and after their intensive care treatment. The primary endpoint was the living conditions as representation of functional status of ICU-survivors before ICU admission and 90-days after ICU discharge. Secondary outcomes were quality of life, maintenance of the functional independence, and the availability of written directives.

2. Methods

2.1. Design and context

This investigation is a component of the COVIP study (COVID-19 in very old intensive care patients), a multinational, multicenter study exploring outcomes in COVID-19 patients aged 70 years and above who required ICU admission (see Supplemental Table 1). The COVIP study operates under the umbrella of the Very Old Intensive Care Patients (VIP) initiative, officially endorsed by the European Society of Intensive Care Medicine (ESICM) (www.vipstudy.org). Registration of the study was completed on ClinicalTrials.gov under the identifier NCT04321265. Adhering to the European Union General Data Privacy Regulation (GDPR) directive, COVIP was conducted ethically and in alignment with the principles of the Declaration of Helsinki. National coordinators facilitated the recruitment of intensive care units (ICUs), managed national and local ethical approvals, and oversaw patient enrolment at the national level, as in the previous VIP studies (6,19,20).

2.2. Study population

Individuals aged 70 years and above who experienced an acute admission to the ICU due to COVID-19 were considered eligible for participation. A screening log was not requested. Recruitment of patients was carried out successively. The dataset utilized in this analysis was retrieved from the COVIP study database on October 15th, 2023, encompassing information on patients admitted to the ICU from March 16th, 2022, to June 19th, 2023. The initiation of data collection coincided with ICU admission, denoted as day one, with subsequent days being systematically numbered in sequential order from this initial date.

2.3. Data collection

Uniform online electronic case report forms (eCRFs) were employed across all participating centers. The initial arterial blood gas (ABG) analysis on admission, incorporating parameters such as pO2 [mmHg] and FiO2 [%], enabled the computation of the pO2/FiO2 ratio. SOFA scores on admission were recorded, and the eCRF automatically calculated the total score. Additionally, the eCRF captured information on ventilation methods, prone positioning, tracheostomy, vasopressor usage, renal replacement therapy, and any limitations on life-sustaining therapy during ICU stay. Withdrawing life sustaining therapy was defined as any decision to withdraw life sustaining therapy that had already been started; withholding life sustaining therapy as any decision to withhold the first life sustaining therapy.

Pre-hospital admission frailty levels were assessed using the Clinical Frailty Scale (CFS) (19,20). Patient demographic information, including sex, age, length of ICU stay, symptom onset, and pre-ICU and hospitalization symptom duration, was documented. Pre-existing comorbidities, such as diabetes, ischemic heart disease, renal insufficiency, arterial hypertension, pulmonary conditions, and chronic heart failure, were also registered. The 90 days follow-up after ICU admission life quality assessment was conducted through the EQ-5D-5L scoring system, with data, which could be collected with telephone interviews, paper inquiries or derived from electronic health records (if such data was collected as part of the normal health care process). The EQ-5D-5L questionnaire is a standardized tool used to measure health-related quality of life covering five dimensions of health: mobility, self-care, usual activities, pain/discomfort, and anxiety/depression. Each of these dimensions is assessed on a scale of five severity levels, ranging from no problems to extreme difficulty. This structure allows for a more detailed understanding of a patient's health status compared to earlier versions, such as the EQ-5D-3L (see Supplements) (18). In addition to the patient's own assessment, the questionnaire can also include input from a caregiver, providing an external perspective on the individual's condition. This caregiver feedback is valuable in situations where patients might have difficulty providing reliable self-reports, such as in cases of cognitive impairment or severe illness. By integrating both the patient's and caregiver's perspectives, the EQ-5D-5L offers a more

comprehensive evaluation of an individual's quality of life. The eCRF and database were securely hosted at Aarhus University, Denmark.

2.4. Statistical analysis

The primary endpoint was the difference of living conditions of ICUsurvivors before ICU admission and 90-days after ICU discharge. Secondary outcomes were 90-days mortality, and quality of life (EQ-5D).

. Continuous data were presented as medians and IQRs, and the Mann-Whitney U test assessed differences between independent groups. Categorical data were expressed as numbers and percentages, and the Chi-square test determined group differences. Marginal predictive means with 95 % confidence intervals (CI) were computed, and Kaplan-Meier differences were tested using the log-rank test. All tests were two-sided, and statistical significance was p < 0.05. Due to incomplete parameter availability for all categories, subgroup analyses necessitated the exclusion of some patients, leading to less than 100 % patient inclusion in specific analyses. Stata 16 (Stata Corp, StataCorp LLC, 4905 Lakeway Drive College Station, Texas 77,845–4512, USA) and SPSS (IBM® SPSS® Statistics, Version 28.0.1.1., IBM, 1 New Orchard Road, Armonk, New York 10,504–1722, United States) as used for statistical computations. The graphical abstract was crafted using BioRender.com.

3. Results

3.1. Specific characteristics of the participating ICUs

In total, 46 ICUs from 13 countries across 3 continents participated in the recruitment (see contributor's list in Supplemental Table 1). The number of recruited patients and the number of participating ICUs varied significantly, with the majority of patients being recruited from Germany, France, and Egypt (see Supplemental Fig. 1). Most contributing ICUs also originated from these countries. A total of 295 patients were recruited from general ICUs, 272 from internal medicine conservative ICUs, and 81 from surgical ICUs. This resulted in substantial variation in treatment algorithms, technical and personnel resources, as well as socio-cultural backgrounds among the ICUs. Detailed information on the average number of beds per country and the availability of ECMO can be found in the Supplemental Tables (Supplemental Table 2). However, data on personnel resources or socio-cultural backgrounds had not been recorded.

3.2. Short-term and 90-days mortality

A total of 642 patients were included (Fig. 1). ICU mortality was 39 % (n = 252), and 30-days mortality 47 % (n = 274). In the follow up 90 days after ICU admission, mortality raised up to 55 % (n = 312). The median age at admission was 77 years (IQR: 73–82). Regarding gender distribution, 60 % (n = 385) were male and 40 % (n = 257) were female. The median SOFA on ICU admission was 5 (IQR: 3–8). Habitat before admission varied: 46 % (n = 293) lived independently in their own homes without support, 33 % (n = 212) lived at home with support, 10



Fig. 1. Consort diagram.

% (n = 65) resided in homes with family or caregivers, 7 % (n = 44) were from nursing homes, 3 % (n = 19) from hospital wards, and 1 % (n = 5) from other places. Vaccination status was as follows: 40 % (n = 242) were unvaccinated, 25 % (n = 152) had received one dose, and 34 % (n = 204) had received two doses. The CFS before acute illness was 4 (IQR: 3–6). The median Horowitz index on ICU admission was 131 (IQR: 83–210).

3.3. Life conditions pre-illness and pre-existing comorbidities

Significantly more ICU survivors lived at their own homes without support before ICU admission than non-survivors (p = 0.016). More non-survivors resided in nursing homes than survivors (p = 0.016). Notably, there was a statistically significant difference in the CFS, with survivors having a lower median score (4 (3–6)) compared to non-survivors (5 (3–6)) (p = 0.007). Sex distribution did not significantly differ between ICU survivors and non-survivors (p = 0.52). In the non-survivor group, a higher proportion (50 %) had not been vaccinated than the ICU survivors (34 %, p < 0.001). Furthermore, in the initial fully vaccinated category, a comparable percentage of non-survivors (25 %) and ICU survivors (26 %) was found. However, a notable distinction emerged in the group that received booster doses, where a significantly lower percentage (24 %) of non-survivors had received boosters compared to the ICU survivors (41 %).

3.4. ICU treatment

Intubation and mechanical ventilation were required for 42% (269), non-invasive ventilation (NIV) in 40 % (257) and high-flow nasal oxygen was used in 37 % (238) of the patients. Prone positioning was used in 18 % (116), and tracheostomy was performed in 7 % (42) of cases. Vasoactive drugs were used in 40 % (254). Renal replacement therapy was administered to 13 % (82). Life-sustaining care was withheld in 25 % (158) of cases and withdrawn in 14 % (87). Family meetings to discuss prognosis, care limitations, and palliative decisions occurred in 55 % (345) of cases. Treatment was withdrawn or withheld due to triage conditions in 4 % (8). 160 patients had available written advance directives (25 %). In 7 % (43) of cases, ICU discharge was planned with a geriatrician, not available in most ICUs that participated in the study (Table 1).

3.5. ICU outcomes

Notable differences in interventions and treatments were observed between survivors and non-survivors: Non-survivors exhibited lower pO2/FiO2 ratios (p < 0.001), significantly higher rates of intubation, mechanical ventilation, and vasoactive drugs (p < 0.001), and renal replacement therapy (p < 0.001, Table 2) at ICU admission. Table 2 summarizes the differences in ICU outcomes: 15 % of ICU survivors and 32 % of non-survivors (p < 0.001) evidenced to have a life-sustaining care withheld, and 2 % of ICU survivors and 32 % of non-survivors (p < 0.001) did have life-sustaining care withdrawn. Regarding communication about ICU treatment, a significant difference was observed (p < 0.001), with 54 % of ICU survivors and 32 % of non-survivors needing a family meeting to discuss prognosis and care limitations (p < 0.001). Only one-quarter of the patients in both groups had any written advanced directives available for the treatment team (26 % (99) versus 24 % (61), p = 0.61). Additional supplemental tables summarize differences regarding the baseline characteristics of patients with and without limitations of life-sustaining therapy (Supplemental Table 3), regarding the frequency of limitations for life-sustaining therapy of the different countries (Supplemental Table 4) and between different living conditions before ICU admittance (Supplemental Table 5).

Table 1

Baseline characteristics before and at ICU-admission including ICU-treatment.

	ICU survivors	ICU non- survivors	p-value
	N = 390 (61 %)	N = 252 (39 %)	
Clinical Frailty Scale [†]	4 (3–6)	5 (3–6)	0.007
Age at admission [years]	[†] 77 (73–82)	78 (74–82)	0.094
Male gender	59 % (230)	62 % (155)	0.52
Days in the hospital before ICU admission*	3 (± 7)	5 (± 9)	0.04
Days with symptoms before ICU admission*	5 (± 5)	6 (± 6)	0.02
Vaccination status			< 0.001
Not vaccinated	34 % (120)	50 % (122)	
Initial fully vaccinated ¹	26 % (91)	25 % (61)	
Received booster	41 % (145)	24 % (59)	
Habitat before admission			0.016
Own home - independent (no support)	49 % (191)	40 % (102)	
Own home (with support)	31 % (119)	37 % (93)	
Other home with family or	8 % (31)	13 % (34)	
caregivers			
Nursing home	8 % (31)	5 % (13)	
Hospital ward	4 % (14)	2 % (5)	
Other	0 % (1)	2 % (4)	
SOFA-Score [†]	4 (3–7)	6 (4–11)	<0.001
FiO2 on admission ^{\dagger}	0.51	0.72 (0.50–1.0)	<0.001
+	(0.35–0.80)		
Horowitz index	148 (94–226)	105 (69–156)	< 0.001
Non-invasive ventilation (NIV)	34 % (133)	49 % (124)	< 0.001
High flow nasal oxygen HFNO	35 % (136)	41 % (102)	0.17
Intubation and mechanical ventilation	24 % (93)	70 % (176)	<0.001
Treatment with prone position	10 % (40)	30 % (76)	< 0.001
Tracheostomy	6 % (22)	8 % (20)	0.27
Vasoactive drugs	29 % (111)	57 % (143)	< 0.001
Renal Replacement Therapy	6 % (25)	23 % (57)	<0.001

Numbers do not result in 100 % due to missing values.

Mean + standard deviation (comparison using student's t-test).

Median + interquartile range (comparison using mann whitney U test), for numbers (percentages) comparison using chi-square test. SOFA Sequential Organ Failure Assessment, FIO2 Fraction of Inspired Oxygen, ICU Intensive Care Unit.

According to license + > 14 days since last vaccination.

3.6. Mortality and functional long-term outcomes after 90 days

Among ICU survivors, 81 % (n = 253) survived at 90 days. In the cohort of patients who survived three months post-ICU admission and participated in the long-term follow-up survey, notable trends were observed regarding their living arrangements. A higher proportion of patients (35 %) resided in their own homes with need for support, reflecting a potential need for assistance in daily activities. However, 35 % of patients lived independently at home without additional support. 4 % resided in other homes with family or caregivers. 14 % needed nursing homes, while 7 % were still in hospital wards. The 90-day outcome differed significantly depending on the individual living conditions before ICU admission. Fig. 3 illustrates that patients who lived at home with their family had a worse long-term mortality than those who lived in a nursing home prior to admission (p = 0.029). Logistic regression analysis revealed a significant association between the living conditions before acute illness and 90-day mortality. However, the overall predictive accuracy of the model was moderate at 58.7 % (see Supplemental Table 6). 22 % of the surviving patients lived in the same living conditions after 90 days (38 % different living conditions, 38 % unknown living conditions).

3.7. ICU treatment from a patient's perspective

After 90 days, patients were asked if they would have chosen to be

Table 2

	ICU survivors	ICU non- survivors	p-value
	N = 390	N = 252	
Life sustaining care withheld ¹ Life sustaining care withdrawn ¹ Was any family meeting performed?	15 % (59) 2 % (6) 46 % (176)	39 % (99) 32 % (81) 68 % (169)	<0.001 <0.001 <0.001
Was treatment withdrawn or withheld in a triage condition (situation) without consulting the family or caregiver?	5 % (3)	4 % (5)	0.77
Were any written advanced directives available for the treatment team?	26 % (99)	24 % (61)	0.61
Length of stay in the ICU [hours] *	221.0 (±301)	274.7 (±285)	0.025
Duration of mechanical ventilation [days]	14 (±15.0)	12(±12.7)	0.108
Day of withholding life sustaining therapy $^{\dagger}1$	1 (1–2)	3 (1–9)	< 0.001
Day of withdrawing life sustaining therapy †	34 (10–37)	8 (3–18)	0.523
30 days mortality	10 % (31)	96 % (243)	<0.001

Mean + standard deviation (comparison using student's t-test).

 $^{\dagger}\,$ Median + interquartile range (comparison using mann whitney U test), for numbers (percentages) comparison using chi-square test.

¹ Limitation of life-sustaining therapy can occur both in terms of withholding and withdrawing therapy in the same patient. ICU = Intensive Care Unit. Numbers do not result in 100 % due to missing values.

treated in the ICU again if they had known what their current condition would be (see Table 3). The majority (58 %) answered positively, but 6 % indicated that they would not have chosen ICU treatment if they had known their current condition in advance, and 37 % were uncertain. Similarly, when the relatives were asked whether they would have chosen ICU admission if they could have known the patient's condition three months in advance, 50 % said yes, 5 % said no, and 44 % were unsure. Notably, there were discordant statements between the patient and his relatives in 46 patients (22 %) of the cases. Similar results were obtained for the statements from the relatives (62.1 \pm 21.2 versus 53.2 \pm 24.3, p = 0.256) and comparing patients with a clear statement to

lable	3		

90-days outcome.	
Mortality after 90 days after ICU admission	19 % (60)
Overall self-reported health status ¹	60
-	(50-75)
Place of living after three months	
Own home - independent (no support)	35 % (85)
Own home (with support)	35 % (86)
Other home with family or caregivers	4 % (10)
Nursing home	14 % (34)
Hospital ward	7 % (17)
Other	1 % (3)
Unknown	3 % (8)
If you had known this would be your current condition after three months: Would you have wanted ICU care?	
No	6 % (12)
Yes	58 %
	(123)
I don't know	37 % (78)
If you had known this would be the patient's condition after three	
months: Would you have wanted ICU care for your relative?	
No	5 % (11)
Yes	50 %

(105)

44 % (93)

EQ-5D-5L: EuroQol Group 5-Dimensionen 5-Level is provided in Supplemental table 2.

¹ Rated on a scale from 0 to 100, with 0 being the worst imaginable health and 100 being the best.

Yes

I don't know

patients with an unclear preference for ICU admission. The complete trajectory is presented in Fig. 2.

3.8. Quality of life after three months

In only 92 cases, EQ-5D-5L scores (39%) were obtained directly from the patients. Regarding mobility, 25% (n = 43) of respondents reported no problems regarding their walking ability, whereas 24% (n = 41) indicated slight difficulties. A comparable percentage, 26% (45), reported moderate problems, while 17% (30) experienced severe problems, and 8% (13) reported an inability to walk about. Regarding selfcare, 45% (78) reported no problems in washing or dressing, while 21% (36) experienced slight difficulties. For usual activities, 28% (48) had no problems, and 30% (51) reported slight problems. Pain and discomfort levels varied, with 42% (73) reporting none, and anxiety or depression was indicated by 52% (89) as being absent. The overall selfreported health status, rated on a scale from 0 to 100, with 0 being the worst imaginable health and 100 being the best, had a median value of 60 (with an interquartile range of 50–75 (see Supplemental Table 7).

4. Discussion

The present study offers new insights into the complete trajectory before, during and after the intensive care treatment of very old intensive care patients suffering from COVID-19 in the post-vaccination era. This is of particular importance because, despite mass vaccination campaigns, infections still occur (1), with age being one of the most prevalent risk factors for a worse outcome (2). The present study highlights important aspects reflecting the old critical care patient's journey starting with the individual living conditions before ICU admission, through the ICU treatment, and 90 days after ICU admission.

Firstly, pre-ICU characteristics significantly impact outcomes. Survivors were more likely to live independently at home and have lower frailty scores. Secondly, there were notable divergences in ICU



Fig. 3. Vital status of patients with different individual living situations before ICU admission. p < 0.001 (Chi-Square).

treatment outcomes between survivors and non-survivors. Non-survivors received more aggressive interventions, including intubation, mechanical ventilation, prone positioning, and increased use of vasoactive drugs and renal replacement therapy. Lastly, the study reveals disparities in end-of-life decisions and communication practices, emphasizing the need for standardized care planning in critical care settings.

In general, old ICU patients deserve special attention (21,22). While ageing constitutes a more comprehensive biological process affecting the entire organism, senescence represents a cellular mechanism that can be initiated by various stimuli, but on which there are more doubts than certainties about the mechanisms involved (23). Growing evidence



Fig. 2. Sankey diagram about the trajectory of old ICU patients suffering from Covid-19 before, during and after ICU-admission.

suggests that critical conditions can activate cell senescence programs regardless of the patient's age (24). This is particularly true for COVID-19 (25). Lee et al. showed that Sars-CoV-2 induces cellular senescence as a primary stress response in infected cells (26). However, the present study did not collect specific data about inflammatory factors to correlate these pathophysiological concepts with clinical outcomes. ICU mortality was 39 %, which is not higher than the outcome in retrospective cohort studies. For example, Kim et al. analysed 542 patients with a mean age of 68 ± 16 years and found a hospital mortality of 39.7 % (27).

Notably, only 25 % (160) of the patients had written advanced directives available for the ICU treatment team. This is significantly lower than the reported percentage in the literature: For example, Sutter et al. found a median of 39 % (IQR: 14–72 %) in their review about neurocritically ill patients (28).

Although many studies focused on ICU- and short-term mortality of VIPs suffering from COVID-19, only few data exist about the long-term mortality of these patients. Hägglöf et al., in a nationwide cohort study, evaluated the 360 days survival outcomes of over 8000 adult COVID-19 patients admitted to Swedish ICUs until August 12, 2022, (29). Their primary focus was on 360-day mortality after ICU admission. The median age of their patients was 63 years, with the majority being men (70.1 %). Among the 7390 patients with complete 360-day mortality data, 24.4 % died within 30 days, 28.8 % within 90 days, and 29.8 % within 360 days from ICU admission. The present study's 90-day mortality was much higher (48.3 %). Of note, most patients who were recorded as "Dead" at the 90-days follow up had already died on the ICU. In discharged patients, mortality was lower but still considerable (19%). This data might emphasize the need for a structured approach to post-ICU care to optimise the long-term outcomes of VIPs, although no detailed data was collected in terms of for example type of rehabilitation. However, there already exists some positive evidence supporting the need for a structured approach after ICU care (30).

In the present study, a geriatrician was involved in ICU discharge in only 36 patients. However, in a recent survey, most ICU physicians recommend involving them in the discharge process (31,32). In a oneyear retrospective cohort study by Sinvani et al., 179 patients (mean age 80.5 years) admitted to a medical intensive care unit and later transferred to the medicine service were analysed. Despite these recommendations, most ICUs, especially in the south of Europe, do not have access to geriatricians on due time. In their study, nonadherence to geriatric-focused practices correlated with an extended stay in the intensive care unit. The authors concluded that despite increased awareness, implementing geriatric-focused practices in intensive care remains inconsistent (33). Notably, patients who lived with their families before ICU admission evidenced significantly higher long-term mortality. However, the causal relationship is questionable, but this association might support a structured approach to aftercare that involves geriatric specialists to help optimise long-term outcomes.

Apart from pure survival (34), quality of life has often been defined as an essential dimension when measuring outcome in critical care. In the present study, there was a small difference between proxies and patients about the question, whether they would have wanted ICU care again when knowing their quality of life 90 days after ICU admittance. Interestingly, patients were more positive about ICU care than their relatives, which is in line with an ICU study by Hofhuis et al. (35). These discrepancies might have a profound impact on decision-making in critical care settings, especially when patients are incapacitated, and families must make decisions on their behalf. This divergence underscores the importance of early and thorough communication between healthcare providers, patients, and their families. Ensuring that families fully understand the prognosis, treatment options, and potential outcomes can help bridge this gap, aligning treatment decisions more closely with the patient's values and preferences. It also highlights the need for proactive advance care planning, where patients can clearly communicate their wishes before they are no longer able to do so,

reducing the emotional burden on families and minimizing the potential for conflicting decisions.

Quality of life in terms of EQ-5D-5L is in line with other studies: Recently, Van der Wal et al. conducted a sub-study of the ICONIC (Conservative versus Liberal Oxygenation Targets in Intensive Care Unit Patients) trial. In ICONIC, 664 patients were enrolled to compare a lowoxygenation strategy to a high-oxygenation strategy in terms of 28-day mortality (36). In the sub-study, depending on the quartile, EQ-5D-index at 6 months ranged from 0.47 (0.29–0.56) for the first quartile to 1 (1) for the fourths quartile (37). It must be noticed that patients in ICONIC were significantly younger than in the present study (ranging from 63 (50–68) to 67 (56–72) years).

Last, quality of life is a crucial outcome measure, particularly in guiding decision-making for vulnerable patient groups. A VAS score of 60 suggests that many patients experience a moderate to low level of perceived well-being, which could indicate significant physical or psychological distress during or after intensive care. Furthermore, the observation that around 40 % of patients and relatives are uncertain about ICU admission highlights a potential lack of confidence or unresolved concerns about the benefits of such care. This uncertainty may serve as an important indicator for clinicians to reconsider how decisions are communicated and to explore ways to better align treatment options with patient preferences and expected quality of life outcomes.

The present study underscores that pre-ICU characteristics, such as independent living and lower frailty scores, significantly impact outcomes, although these differences were small, and the clinical implication is unknown. However, the crude differences in ICU treatment requirements between survivors and non-survivors, with non-survivors undergoing more invasive interventions, suggest that aggressive ICU care may not always lead to improved outcomes in this population. The high mortality rate in our cohort-48.3 % at 90 days-demonstrates the vulnerability of older ICU patients, reinforcing the importance of structured post-ICU care and rehabilitation to improve long-term outcomes. Furthermore, the observed variability in end-of-life decisions and communication practices indicates a critical need for standardized approaches to care planning that involve patients and their families early in the ICU admission process. Addressing this gap could help alleviate the uncertainty that 40 % of patients and relatives experience regarding ICU admission, ensuring that care aligns with their values and expected quality of life. These findings suggest that when admitting older COVID-19 patients to the ICU, clinicians should not only consider immediate survival but also the broader implications for long-term recovery, functional status, and quality of life. More structured apincluding geriatric involvement proaches, and improved communication about the risks and benefits of ICU care, are essential to optimizing outcomes for this vulnerable population. All this raises important questions about the appropriateness of certain treatments in old and very old patients and underscores the need for individualized, patient-centred decision-making that considers not only survival but also post-ICU quality of life.

4.1. Limitations

Our analysis is limited by the absence of certain data in the COVIP database, including details about individual adherence to guidelines, specific medical treatments, or device therapy. However, this focused approach on key information was deliberate to prevent the database from becoming heterogeneous and inaccurate due to the involvement of numerous centers (31). Similar to other COVIP studies, our research shares methodological constraints, such as the absence of a control group of younger COVID-19 patients for comparison and the lack of a comparable age cohort not admitted to the ICU (6,38–42). In fact, around about half of critically ill old patients suffering from COVID-19 are not admitted to an ICU due to the early limitation of life-sustaining therapy (43). Additionally, the COVIP database lacks information on pre-ICU care and triage, potentially influencing the care of

older ICU patients. The diverse care structures across the 26 participating countries contribute to significant heterogeneity in treatment approaches (44). Despite this limitation, the varied care settings also represent a notable strength of the database, offering a comprehensive perspective rather than selective data from a specific level of care. Another limitation is that we do not know how many patients developed ventilator-associated pneumonia with bacterial super-infection, which occurs frequently and constitutes an established risk factor for worse outcomes (45). In addition, we observed a relatively high number of lost to follow up cases. Last, in this study, patients were enrolled sequentially from all participating ICU units without utilizing a screening log to systematically identify eligible individuals. This approach limits the ability to evaluate how well the sample represents potential confounders or the broader ICU patient population. Therefore, although the data offer important insights into the traits and outcomes of patients in the recruited ICUs, it is important to be cautious when applying these findings to a broader context. Future studies that adopt a more systematic recruitment process, including the use of a screening log, could improve the applicability of the results to a wider audience.

5. Conclusion

In conclusion, this study contributes valuable insights into the multifaceted aspects of care for older COVID-19 patients admitted late in the pandemic with an average degree of complete vaccinations, encompassing pre-ICU characteristics, treatment outcomes, end-of-life decisions, mortality, and long-term quality of life. While age did not differ between ICU survivors and non-survivors, frailty was significantly lower in survivors. Living conditions had an impact on survival. Only a minority of patients returned after ICU survival to the same living conditions as before ICU admittance. Interestingly, we found a significant number of patients who died after ICU discharge before 90 days of follow up. In addition, many patients experience a moderate to low level of quality of life, although patients were more positive about ICU care than their relatives. The findings emphasize the necessity of a standardized and patient-centered approach in critical and post-ICU settings to optimise outcomes and enhance the overall quality of care for this vulnerable population.

Ethical statements

The primary competent ethics committee was the Ethics Committee of the University of Duesseldorf, Germany. Institutional research ethics board approval was obtained from each study site.

Funding

This study was endorsed by the ESICM. Free support for running the electronic database was granted from the dep. of Epidemiology, University of Aarhus, Denmark. The support of the study in France by a grant from "Fondation Assistance Publique-Hôpitaux de Paris pour la recherche" is greatly appreciated. In Norway, the study was supported by a grant from the Health Region West. In addition, the study was supported by a grant from the European Open Science Cloud (EOSC). EOSCsecretariat.eu has received funding from the European Union's Horizon Programme call H2020-INFRAEOSC-05-2018-2019, grant agreement number 831644. This work was supported by the Forschungskommission of the Medical Faculty of the Heinrich-Heine-University Düsseldorf, No. 2020–21 to RRB for a Clinician Scientist Track.

CRediT authorship contribution statement

Raphael Romano Bruno: Writing – review & editing, Writing – original draft, Visualization, Validation, Software, Resources, Project administration, Methodology, Investigation, Formal analysis, Data curation, Conceptualization. **Bernhard Wernly:** Conceptualization.

Antonio Artigas: Resources. Kristina Fuest: Writing – review & editing. Stefan J. Schaller: Conceptualization. Lisa Dannenberg: Writing – review & editing. Detlef Kindgen-Milles: Data curation. Malte Kelm: Conceptualization. Michael Beil: Data curation. Sigal Sviri: Resources. Muhammed Elhadi: Resources. Michael Joannidis: Investigation. Sandra Oeyen: Conceptualization. Eumorfia Kondili: Conceptualization. Rui Moreno: Conceptualization. Susannah Leaver: Supervision, Conceptualization. Bertrand Guidet: Resources, Conceptualization. Dylan W. De Lange: Resources. Hans Flaatten: Conceptualization. Wojciech Szczeklik: Conceptualization. Christian Jung: Writing – review & editing, Visualization, Validation, Supervision, Resources, Project administration, Methodology, Investigation, Funding acquisition, Formal analysis, Data curation, Conceptualization.

Declaration of competing interest

SJS received grants and non-financial support from Reactive Robotics GmbH (Munich, Germany), ASP GmbH (Attendorn, Germany), STIMIT AG (Biel, Switzerland), ESICM (Geneva, Switzerland), grants, personal fees, and non-financial support from Fresenius Kabi Deutschland GmbH (Bad Homburg, Germany), grants from the Innovationsfond of The Federal Joint Committee (G-BA), personal fees from Springer Verlag GmbH (Vienna, Austria) for educational purposes and Advanz Pharma GmbH (Bielefeld, Germany), non-financial support from national and international societies (and their congress organisers) in the field of anesthesiology and intensive care medicine, outside the submitted work. Dr. Schaller holds stocks in small amounts from Alphabet Inc., Bayer AG, and Siemens AG; these holdings have not affected any decisions regarding his research or this study.

All other authors declare that they have no competing interests.

Data availability

Individual participant data that underlie the results reported in this article are available to investigators whose proposed use of the data has been approved by the COVIP steering committee. The anonymised data can be requested from the authors if required.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.jcrc.2024.154984.

References

- Ticinesi A, Nouvenne A, Parise A, Prati B, Meschi T. Defining SARS-CoV-2 breakthrough infection needing hospitalization in mass vaccination era: from disease-centered to patient-centered care. Acta Biomed. 2022;93(2):e2022182.
- [2] Bajci MP, Lendak DF, Ristic M, Drljaca MM, Brkic S, Turkulov V, et al. COVID-19 breakthrough infections among patients aged >/=65 years in Serbia: morbidity and mortality overview. Vaccines (Basel). 2022;10(11).
- [3] Guidet B, Jung C, Flaatten H, Fjolner J, Artigas A, Pinto BB, et al. Increased 30-day mortality in very old ICU patients with COVID-19 compared to patients with respiratory failure without COVID-19. Intensive Care Med. 2022;48(4):435–47.
- [4] Armstrong RA, Kane AD, Cook TM. Outcomes from intensive care in patients with COVID-19: a systematic review and meta-analysis of observational studies. Anaesthesia 2020;75(10):1340–9.
- [5] Bellelli G, Rebora P, Valsecchi MG, Bonfanti P, Citerio G, members C-MT.. Frailty index predicts poor outcome in COVID-19 patients. Intensive Care Med. 2020;46 (8):1634–6.
- [6] Jung C, Flaatten H, Fjolner J, Bruno RR, Wernly B, Artigas A, et al. The impact of frailty on survival in elderly intensive care patients with COVID-19: the COVIP study. Crit. Care 2021;25(1):149.
- [7] Jung C, Bruno RR, Jumean M, Price S, Krychtiuk KA, Ramanathan K, et al. Management of cardiogenic shock: state-of-the-art. Intensive Care Med 2024;50: 1814–29.
- [8] Wernly B, Flaatten H, Leaver S, Guidet B, Jung C, investigators C.. The clinical frailty scale, but not the FRAIL checklist is associated with mortality in old critically ill patients with COVID-19. Crit. Care 2023;27(1):101.
- [9] Wernly B, Flaatten H, Leaver S, Guidet B, Jung C, investigators C.. Improving frailty assessment: the task is not finished. Crit. Care 2023;27(1):218.

R.R. Bruno et al.

- [10] Bruno RR, Wernly B, Wolff G, Fjolner J, Artigas A, Bollen Pinto B, et al. Association of chronic heart failure with mortality in old intensive care patients suffering from Covid-19. ESC Heart Fail. 2022;9(3):1756–65.
- [11] Mayerhofer T, Klein S, Wernly B, Flaatten H, Guidet B, De Lange DW, et al. Diabetes mellitus is associated with 90-day mortality in old critically ill COVID-19 patients: a multicenter prospective observational cohort study. Infection 2023;51 (5):1407–15.
- [12] Bruno RR, Wernly B, Flaatten H, Fjolner J, Artigas A, Baldia PH, et al. The association of the activities of daily living and the outcome of old intensive care patients suffering from COVID-19. Ann. Intensive Care 2022;12(1):26.
- [13] Wolff G, Wernly B, Flaatten H, Fjolner J, Bruno RR, Artigas A, et al. Sex-specific treatment characteristics and 30-day mortality outcomes of critically ill COVID-19 patients over 70 years of age-results from the prospective COVIP study. Can. J. Anaesth. 2022;69(11):1390–8.
- [14] Wernly B, Rezar R, Flaatten H, Beil M, Fjolner J, Bruno RR, et al. Variations in endof-life care practices in older critically ill patients with COVID-19 in Europe. J. Intern. Med. 2022;292(3):438–49.
- [15] Ibarz M, Haas LEM, Ceccato A, Artigas A. The critically ill older patient with sepsis: a narrative review. Ann. Intensive Care 2024;14(1):6.
- [16] Polok K, Fronczek J, Artigas A, Flaatten H, Guidet B, De Lange DW, et al. Noninvasive ventilation in COVID-19 patients aged >/= 70 years-a prospective multicentre cohort study. Crit. Care 2022;26(1):224.
- [17] Polok K, Fronczek J, Guidet B, Artigas A, De Lange DW, Fjolner J, et al. Outcomes of patients aged >/=80 years with respiratory failure initially treated with noninvasive ventilation in European intensive care units before and during COVID-19 pandemic. Ann. Intensive Care 2023;13(1):82.
- [18] Soliman IW, Leaver S, Flaatten H, Fjolner J, Wernly B, Bruno RR, et al. Healthrelated quality of life in older patients surviving ICU treatment for COVID-19: results from an international observational study of patients older than 70 years. Age Ageing 2022;51(2).
- [19] Flaatten H, De Lange DW, Morandi A, Andersen FH, Artigas A, Bertolini G, et al. The impact of frailty on ICU and 30-day mortality and the level of care in very elderly patients (>/= 80 years). Intensive Care Med. 2017;43(12):1820–8.
- [20] Guidet B, de Lange DW, Boumendil A, Leaver S, Watson X, Boulanger C, et al. The contribution of frailty, cognition, activity of daily life and comorbidities on outcome in acutely admitted patients over 80 years in European ICUs: the VIP2 study. Intensive Care Med. 2020;46(1):57–69.
- [21] Martin-Vicente P, Lopez-Martinez C, Rioseras B, Albaiceta GM. Activation of senescence in critically ill patients: mechanisms, consequences and therapeutic opportunities. Ann. Intensive Care 2024;14(1):2.
- [22] Guidet B, Vallet H, Flaatten H, Joynt G, Bagshaw SM, Leaver SK, et al. The trajectory of very old critically ill patients. Intensive Care Med. 2024;50(2): 181–94.
- [23] Munoz-Espin D, Serrano M. Cellular senescence: from physiology to pathology. Nat. Rev. Mol. Cell Biol. 2014;15(7):482–96.
- [24] Chen C, Zheng M, Hou H, Fang S, Chen L, Yang J, et al. Cellular senescence in ischemia/reperfusion injury. Cell Death Discov. 2022;8(1):420.
- [25] Schmitt CA, Tchkonia T, Niedernhofer LJ, Robbins PD, Kirkland JL, Lee S. COVID-19 and cellular senescence. Nat. Rev. Immunol. 2023;23(4):251–63.
- [26] Lee S, Yu Y, Trimpert J, Benthani F, Mairhofer M, Richter-Pechanska P, et al. Virusinduced senescence is a driver and therapeutic target in COVID-19. Nature 2021; 599(7884):283–9.
- [27] Kim S, Choi H, Sim JK, Jung WJ, Lee YS, Kim JH. Comparison of clinical characteristics and hospital mortality in critically ill patients without COVID-19 before and during the COVID-19 pandemic: a multicenter, retrospective, propensity score-matched study. Ann. Intensive Care 2022;12(1):57.

- [28] Sutter R, Meyer-Zehnder B, Baumann SM, Marsch S, Pargger H. Advance directives in the neurocritically ill: a systematic review. Crit. Care Med. 2020;48(8):1188–95.
- [29] Hagglof E, Bell M, Zettersten E, Engerstrom L, Larsson E. Long-term survival after intensive care for COVID-19: a nationwide cohort study of more than 8000 patients. Ann. Intensive Care 2023;13(1):76.
- [30] Bloom SL, Stollings JL, Kirkpatrick O, Wang L, Byrne DW, Sevin CM, et al. Randomized clinical trial of an ICU recovery pilot program for survivors of critical illness. Crit. Care Med. 2019;47(10):1337–45.
- [31] Guidet B, Vallet H, Boddaert J, de Lange DW, Morandi A, Leblanc G, et al. Caring for the critically ill patients over 80: a narrative review. Ann. Intensive Care 2018;8 (1):114.
- [32] Vallet H, Guidet B, Boumendil A, De Lange DW, Leaver S, Szczeklik W, et al. The impact of age-related syndromes on ICU process and outcomes in very old patients. Ann. Intensive Care 2023;13(1):68.
- [33] Sinvani L, Kozikowski A, Patel V, Mulvany C, Talukder D, Akerman M, et al. Nonadherence to geriatric-focused practices in older intensive care unit survivors. Am. J. Crit. Care 2018;27(5):354–61.
- [34] Suter P, Armaganidis A, Beaufils F, Bonfill X, Burchardi H, Cook D, et al. Predicting outcome in ICU patients. Intensive Care Med. 1994;20(5):390–7.
- [35] Hofhuis J, Hautvast JLA, Schrijvers AJP, Bakker J. Quality of life on admission to the intensive care: can we query the relatives? Intensive Care Med. 2003;29(6): 974–9.
- [36] van der Wal LI, Grim CCA, Del Prado MR, van Westerloo DJ, Boerma EC, Rijnhartde Jong HG, et al. Conservative versus Liberal oxygenation targets in intensive care unit patients (ICONIC): a randomized clinical trial. Am. J. Respir. Crit. Care Med. 2023;208(7):770–9.
- [37] van der Wal LI, Grim CCA, Del Prado MR, van Westerloo DJ, Schultz MJ, Helmerhorst HJF, et al. Perspectives of ICU patients on deferred consent in the context of post-ICU quality of life: a substudy of a randomized clinical trial. Crit. Care Med. 2024 May 1;52(5):694–703.
- [38] Jung C, Fjolner J, Bruno RR, Wernly B, Artigas A, Bollen Pinto B, et al. Differences in mortality in critically ill elderly patients during the second COVID-19 surge in Europe. Crit. Care 2021;25(1):344.
- [39] Bruno RR, Wernly B, Hornemann J, Flaatten H, FjOlner J, Artigas A, et al. Early evaluation of organ failure using MELD-XI in critically ill elderly COVID-19 patients. Clin. Hemorheol. Microcirc. 2021;79(1):109–20.
- [40] Jung C, Bruno RR, Wernly B, Joannidis M, Oeyen S, Zafeiridis T, et al. Inhibitors of the renin-angiotensin-aldosterone system and COVID-19 in critically ill elderly patients. Eur Heart J Cardiovasc Pharmacother. 2021;7(1):76–7.
- [41] Bruno RR, Wernly B, Flaatten H, Fjolner J, Artigas A, Bollen Pinto B, et al. Lactate is associated with mortality in very old intensive care patients suffering from COVID-19: results from an international observational study of 2860 patients. Ann. Intensive Care 2021;11(1):128.
- [42] Jung C, Wernly B, Fjolner J, Bruno RR, Dudzinski D, Artigas A, et al. Steroid use in elderly critically ill COVID-19 patients. Eur. Respir. J. 2021 Oct 7;58(4):2100979.
- [43] Piers R, Van Braeckel E, Benoit D, Van Den Noortgate N. Early resuscitation orders in hospitalized oldest-old with COVID-19: a multicenter cohort study. Palliat. Med. 2021;35(7):1288-94
- [44] Flaatten H, deLange D, Jung C, Beil M, Guidet B. The impact of end-of-life care on ICU outcome. Intensive Care Med 2021 May:47(5):624–5.
- [45] Laurichesse G, Schwebel C, Buetti N, Neuville M, Siami S, Cohen Y, et al. Mortality, incidence, and microbiological documentation of ventilated acquired pneumonia (VAP) in critically ill patients with COVID-19 or influenza. Ann. Intensive Care 2023;13(1):108.