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Long-term physical impairments in survivors of COVID-19-associated ARDS compared with classic ARDS: A two-center study

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ABSTRACT

Purpose: This work aimed to compare physical impairment in survivors of classic ARDS compared with COVID-19–associated ARDS (CARDS) survivors.

Material and methods: This is a prospective observational cohort study on 248 patients with CARDS and compared them with a historical cohort of 48 patients with classic ARDS. Physical performance was evaluated at 6 and 12 months after ICU discharge, using the Medical Research Council Scale (MRCss), 6-min walk test (6MWT), handgrip dynamometry (HGD), and fatigue severity score (FSS). We also assessed activities of daily living (ADLs) using the Barthel index.

Results: At 6 months, patients with classic ARDS had lower HGD (estimated difference [ED]: 11.71 kg, $p < 0.001$; ED 31.9% of predicted value, $p < 0.001$), 6MWT distance (ED: 89.11 m, $p < 0.001$; ED 12.96% of predicted value, $p = 0.032$), and more frequent significant fatigue (OR 0.35, $p = 0.046$). At 12 months, patients with classic ARDS had lower HGD (ED: 9.08 kg, $p = 0.0014$; ED 25.9% of predicted value, $p < 0.001$) and no difference in terms of 6MWT and fatigue. At 12 months, patients with classic ARDS improved their MRCss (ED 2.50, $p = 0.006$) and HGD (ED: 4.13 kg, $p = 0.002$; ED 9.45% of predicted value, $p = 0.005$), while those with CARDS did not. Most patients in both groups regained independence in ADLs at 6 months.

COVID-19 diagnosis was a significant independent predictor of better HGD ($p < 0.0001$) and 6MWT performance ($p = 0.001$), and lower prevalence of fatigue ($p = 0.018$).

Conclusions: Both classic ARDS and CARDS survivors experienced long-term impairments in physical functioning, confirming that post-intensive care syndrome remains a major legacy of critical illness. Surprisingly, however, persisting disability was more common in survivors of classic ARDS than in CARDS survivors. In fact, muscle strength measured with HGD was reduced in survivors of classic ARDS compared to CARDS patients at both 6 and 12 months. The 6MWT was reduced and fatigue was more common in classic ARDS compared to CARDS at 6 months but differences were no longer significant at 12 months. Most patients in both groups regained independent function in ADLs at 6 months.

Abbreviations: ARDS, Acute respiratory distress syndrome; CARDS, COVID-19–associated ARDS; 6MWT, 6-min walk test; MRCss, Medical Research Council sum score; HGD, handgrip dynamometry; ICU, intensive care unit; NIV, noninvasive ventilation; FSS, fatigue severity score; GLMM, generalized linear mixed model; SAPS II, Simplified Acute Physiology Score II.

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1. Introduction

Survivors of acute respiratory distress syndrome (ARDS) frequently experience long-lasting physical impairments, including muscle weakness and reduced exercise capacity, with decreased quality of life [1-3]. Cognitive and mental health impairments are also commonly reported. This constellation of impairments referred to as post-intensive care syndrome persists beyond acute hospitalization and adversely affects survivors' quality of life [4]. Patients with coronavirus disease 2019 (COVID-19)–associated ARDS (CARDS) may have lengthy intensive care unit (ICU) stays, prolonged mechanical ventilation, protracted use of sedative drugs and neuromuscular blocking agents, and extrapulmonary organ dysfunction [5], suggesting that they also may suffer the same long-term consequences as survivors of non-COVID-19–associated ARDS (classic ARDS). There is a paucity of data on long-term sequelae in survivors of CARDS [6-10]. In a previous study, we found that CARDS leads to persistent physical impairment; however, performance on the 6-min walk test (6MWT) was less impaired, and muscle weakness and fatigue were less prevalent compared with the historical published series of classic ARDS cases [11]. To our knowledge, there are no studies comparing long-term physical performance in patients with classic ARDS and CARDS, with an in-person evaluation at follow-up. In this two-center study, the primary objective was to compare the long-term physical impairments in CARDS and classic ARDS survivors, using a comprehensive array of objective and patient-reported measures of physical function.

2. Materials and methods

This prospective observational cohort study compared patients with CARDS to a historical cohort of patients with classic ARDS. This study was conducted in two large academic hospitals (ASST Spedali Civili di Brescia, Brescia, and ASST San Gerardo Hospital, Monza) in the Lombardy region of northern Italy. Both ICUs are mixed general units with a strong commitment to implementing evidence-based treatments, including the ABCDEF bundle, although implementation rates for the ABCDEF bundle were low during the first pandemic wave. The Ethics Committees of each hospital approved the study. Written informed consent was obtained from each participant during the follow-up visit. We adhered to the STROBE reporting guidelines. [13] This study was registered at ClinicalTrial.gov (NCT: NCT04608994).

2.1. Historical cohort selection

Since 2017, at ASST Spedali Civili di Brescia, a follow-up clinic has been available to evaluate all ICU patients discharged alive from the hospital, with an in-person evaluation of physical, cognitive, and mental impairments. From the available dataset, all critically ill adult (>18 yo) patients with the following inclusion criteria served as the historical classic ARDS cohort: (1) admitted to the ICU from January 27th, 2017 to January 7th, 2020, at ASST Spedali Civili di Brescia; (2) admitted for hypoxemic ARDS; and (3) mechanically ventilated for at least 48 h. Exclusion criteria were: (1) patients that were unable to participate in the follow-up functional examination, (2) patients that did not consent to participate in the study, and (3) patients with a pre-existing neurological condition.

2.2. CARDS cohort selection

The follow-up clinic continues to evaluate the patients during the pandemic period, with some limitations due to the social restrictions during the pandemic. Starting from the end of 2019, the follow-up clinic became multicentric, including, among others, ASST Monza hospital, the only one able to include patients with CARDS.

We enrolled all adult (>18 yo) patients with CARDS who met the following inclusion criteria: (1) admitted to the ICU from February 20th, 2020 to May 5th, 2021, and discharged alive from the hospital; (2) PCR-confirmed SARS-CoV-2 infection; (3) had COVID-19–associated ARDS; and (4) received invasive mechanical ventilation for >48 h. ARDS was defined according to the Berlin definition [12]. Exclusion criteria were the same as the historical cohort.

Demographic (age, sex, and BMI) and clinical data (simplified acute physiology score II, PaO_2/FiO_2 ratio at ICU admission, use of noninvasive ventilation (NIV, including high flow nasal cannula, continuous positive airway pressure [CPAP] and bilevel positive airway pressure [BiPAP]) pre-ICU admission, duration of mechanical ventilation, use of inhaled nitric oxide, the rate of the prone position, the use of extracorporeal membrane oxygenation, tracheostomy, use of steroids in the ICU, continuous veno-venous hemofiltration, vasopressor, the number of comorbidities, ICU stay, and hospital length of stay) were collected. All patients were treated in the ICUs according to the best clinical practice available, including the ABCDEF bundle.

2.3. Follow-up protocol and measurement

Each patient included was scheduled for an outpatient examination at the follow-up clinic of the enrolling hospital at 6 and 12 months after ICU discharge. A detailed description of the follow-up protocol has been published elsewhere [11]. Briefly, an intensivist with nurse assistance assessed muscle weakness using the Medical Research Council Sum Score (MRCss) and handgrip dynamometry (HGD). Activity limitation was evaluated by 6MWT, as a performance-based measure, and fatigue severity score (FSS). For HGD and the 6MWT, predicted values were calculated using existing equations. [8,9] The Barthel index, an ordinal scale that measures the subject's capacity to perform 10 basic activities of daily living (ADLs), was used to evaluate the patients performance in ADLs [14]. This index gives a quantitative estimation of the patient's activity level and ability to perform routine tasks on their own (e.g., grooming, toilet use, dressing, etc.). Scores range from 0 to 100, with higher scores indicating that the patients are more independent and more likely to function with little to no assistance. We categorized the Barthel Index as follows: 80–100 (Independent); 60–79 (Minimally dependent); 40–59 (Partially dependent); 20–39 (Very dependent) and < 20 (Totally dependent).

2.4. Statistical analysis

Quantitative variables are summarized using median and interquartile range (IQR) or mean and standard deviation (SD), while categorical variables are reported as counts and percentages. Linear regression or logistic regression was used to evaluate the differences in terms of acute-phase variables (in the ICU) between classic ARDS and CARDS.

The relationship between physical performance variables as dependent variables, time (6 and 12 months from discharge), and the type of ARDS (classic versus CARDS) as independent variables was modeled using generalized linear mixed models (GLMMs). All unadjusted models were fit assuming only random intercepts (subjects) and included types of ARDS (classic ARDS and CARDS), the follow-up visit time (6 and 12 months), and their interaction as fixed effects. *P*-values for post-hoc comparisons between the ARDS groups at each follow-up time point were adjusted using the Bonferroni method.

Adjusted analysis was carried out using a GLMM to correlate the dependent variable (6MWT, HGD, and FSS) to COVID-19 infection, adjusting for time (6 and 12 months), patient's related factors (age and sex), and the acute-phase confounders that were statistically significant during the ICU stay between the two groups (CARDS and classic ARDS), excluding PaO_2/FiO_2 ratio (already contained in SAPS II); the subject was used as random effects. No data imputation was performed. Statistical significance was defined as p-value <0.05. All analyses were conducted using R (version 4.1.1).

3. Results

Two hundred and forty-eight patients with CARDS (100 patients from ASST Monza and 148 patients from ASST Spedali Civili) were visited at the follow-up clinics and were compared with 48 patients with classic ARDS. Sixty-seven patients with CARDS and 27 with classic ARDS were subsequently visited at 12 months **(Supplementary Fig. 1)**. Comparing patients with classic ARDS to those with CARDS, they were more frequently male (97.9% vs 75.0%, $p < 0.001$), and there were no differences in terms of age (median [IQR]: 66 [58–73] vs 62 [55–68], $p = 0.369$) and BMI (median [IQR]: 27 [23−30] vs 29 [26–32], $p = 0.410$) (Table 1).

At ICU admission, the proportion of patients with moderate and severe ARDS was higher in patients with CARDS ($p = 0.002$) and they more often received NIV ($p < 0.001$). During the ICU stay, patients with CARDS received steroids and pronation more often ($p < 0.001$). Simplified acute physiology score disease severity (SAPS II) was higher in patients with classic ARDS (Table 1).

Concerning the comparison between CARDS and classic ARDS at 6 months, HDG was lower in patients with classic ARDS than in CARDS had lower HGD (estimate difference [ED] in absolute values: 11.71 kg, $p < 0.001$; ED as a percentage of the predicted value: 31.9%, $p < 0.001$) and 6MWT distance (ED in absolute values: 89.11 m, $p < 0.001$; ED as a percentage of the predicted value: 12.96%, $p = 0.032$) and more frequently experienced significant fatigue (OR 0.35 for CARDS, $p = 0.046$) (**Supplementary Table 1**). Patients from both cohorts had normal or mildly reduced muscle strength (measured by MRCss) and were independent in ADLs (Table 2). At 12 months, patients with classic ARDS had a lower HGD (ED in absolute values: 9.08 kg, $p = 0.0014$; ED as a percentage of the predicted value: 25.9%, $p < 0.001$), whereas there was no difference in terms of the 6MWT and fatigue.

Concerning the comparison between 6 months and 12 months in each group, patients with classic ARDS improved their MRCss (ED 2.50, $p = 0.006$) and HGD (ED in absolute values: 4.13, $p = 0.002$; ED as a percentage of the predicted value: 9.45%, $p = 0.005$) at 12 months (Table 2**, Supplementary Table 1**), while patients with CARDS did not further improve their performance at 12 months.

In the adjusted multivariable mixed-model analysis, the estimate difference in classic ARDS patients between 12 months and 6 months indicated that dominant handgrip strength improved over time by 3.98 Kg (9.73%) (Table 3); the 6MWT and fatigue did not change significantly. Estimate difference in classic ARDS patients compared to CARDS patients indicated that dominant handgrip strength increased in CARDS by 12.70 Kg (29.88%), 6MWT increased by 90.23 m (10.91%) and fatigue prevalence decreased by 78% (Table 3**)**.

Moreover, prone positioning, steroids, vasopressor administration during the ICU stay, ICU length of stay, and COVID diagnosis were constantly retained in the model as significant independent predictors for HGD ($p < 0.0001$), 6MWT ($p = 0.001$), and presence of fatigue ($p = 0.018$) (Table 3**)**.

Table 1
Demographic and clinical characteristics of the study population.

	Classic ARDS ($N = 48$)[a]	CARDS (N = 248)[a]	*P*-value
BMI, median (IQR), Kg/m^2	27 (23−30)	29 (26–32)	0.410
Gender, No (%) of Male	47 (97.9%)	186 (75.0%)	<0.001
Age, median (IQR), y	66 (58–73)	62 (55–68)	0.359
SAPS II, median (IQR)	35 (29–48)	31 (27–38)	0.011
PaO2/FiO2 ratio at ICU admission, No (%)			0.002
200–299	8 (16.7%)	9 (3.6%)	
100–199	20 (41.7%)	120 (48.4%)	
<100	20 (41.7%)	119 (48.0%)	
Use of NIV pre-ICU admission - No (%)	22 (45.8%)	202 (81.5%)	<0.001
Duration of mechanical ventilation (days), median (IQR)	9.0 (5.0–14)	10 (6.0–16)	0.523
Inhaled nitric oxide, No of patients (%)	1 (2.1%)	10 (4.0%)	0.813
Prone position, No of patients (%)	3 (6.3%)	128 (51.6%)	<0.001
ECMO, No of patients (%)	2 (4.2%)	8 (3.2%)	0.99
Tracheostomy, No of patients (%)	16 (33.3%)	75 (30.2%)	0.84
Steroids in ICU, No of patients (%)	11 (22.9%)	170 (68.5%)	<0.001
CVVH, No of patients (%)	2 (4.2%)	7 (2.8%)	0.970
Use of vasopressor in ICU, No of patients (%)	24 (50.0%)	79 (31.9%)	0.024
Comorbidities, No (%)			
0	3 (6.3%)	36 (14.5%)	0.292
1	18 (37.5%)	73 (29.4%)	
2	8 (16.7%)	52 (21.0%)	
3	10 (20.8%)	34 (13.7%)	
≥4	9 (18.8%)	33 (13.3%)	
ICU LOS (days), median (IQR)	11 (6.8–16)	13 (8.0–22)	0.057
Hospital LOS (days), median (IQR)	27 (14–45)	32 (22–47)	0.425

List of abbreviations: ARDS: Acute Respiratory Distress Syndrome; CARDS: COVID-related Acute Respiratory Distress Syndrome; BMI, Body Mass Index; IQR, Interquartile Range; SAPS II, Simplified Acute Physiology Score II. ICU, Intensive Care Unit; LOS = length of stay; ECMO, Extra-Corporeal Membrane Oxygenation; NIV, Non-Invasive Ventilation. CVVH, Continuous Veno-Veno hemofiltration; LOS, Length of stay.

[a] Unknown or missing data (No. of patients with missing data, classical ARDS - CARDS): BMI, 3–80; SAPS II, 0–18; Duration of Mechanical Ventilation, 7–5; Tracheostomy, 0–3; Steroids in ICU, 0–24; Number of Comorbidities, 0–20; ICU LOS, 0–13; Hospital LOS, 0–1.

4. Discussion

To the best of our knowledge, this is the first study comparing physical impairments with an in-person physical evaluation in both patients with classic ARDS and CARDS. At 6 months, we found that long-term physical impairments, in terms of dominant-hand grip strength, 6MWT, and presence of fatigue, were significantly more prevalent in survivors of classical ARDS compared with CARDS survivors, independent of other patients- or illness-related factors that could affect long-term outcomes. At 12 months, classic ARDS survivors had persistently lower HGD, but 6MWT, MRCss, and fatigue were comparable to CARS survivors. Most patients in both groups were independent in daily life activities.

The physical performance reported in our populations with classic ARDS and with CARDS is in line with the literature. The percentage predicted 6MWT results of patients with classic ARDS in our population (72% at 6 months and 75% at 12 months) parallel those previously reported by Herridge et al. [2] and Needham et al. [1] (64% at 6 months and 66% at 1 year). We reported clinically significant fatigue in 60% of patients with classic ARDS at 12 months, in line with Neufeld et al. [15] (67% at 12 months). The reported percentages of predicted hand grip strength in our population (mean value of 50% at 6 months and 59% at 12 months) were slightly lower than those reported by Needhale et al. (76% at 6 months and 84% at 12 months). Concerning patients with CARDS, we reported a percentage of the predicted 6MWT of 85% at 6 months, in line with Huang et al. [16] (85% at 6 months in patients requiring mechanical ventilation). Two other published papers [17,18] report higher absolute 6MWT values, with no correction for age and sex; they are difficult to compare with our population. To our knowledge, there are no other in-person evaluations of hand grip strength and fatigue in survivors of CARDS with up to 1-year follow-up. It should be noted that, although fatigue was less prevalent in patients with CARDS, one-third of them still report fatigue at 1 year and their hand grip strength remained impaired (82.5% of predicted value), with no improvement at 6 and 12 months.

A few reports have compared the physical performance of patients with classic ARDS vs CARDS. A secondary analysis of the ISARIC4C Clinical Characterisation Protocol – United Kingdom (CCP-UK) cohort study and the Rehabilitation Complex Intervention for Patients Following Intensive Care Discharge (RECOVER) trial found that fatigue was significantly more common and severe in classic ARDS than in

Table 2
Physical function outcomes in patients with classic ARDS compared with patients with COVID-19 associated ARDS (CARDS).

	6 months		12 Months		p-value[c]
	Classic ARDS[d] (*N* = 44)	CARDS[d] (*N* = 248)	Classic ARDS[d] (*N* = 27)	CARDS[d] (*N* = 67)	
MRCss, median (IQR)	60 (56–60)	60 (60–60)	60 (60–60)	60 (60–60)	P1 = 0.011/ P2 = 0.001/ P3 = 0.004
Dominant-hand grip strength, (kg), median (IQR)	22 (13–24)	33 (24–41)	25 (16–32)	34 (27–40)	P1 < 0.001/ P2 < 0.001/ P3 = 0.034
Dominant-hand grip strength (% predicted), mean (SD)[a]	50.0 (20.1)	83.0 (20.9)	58.9 (24.1)	82.5 (20.0)	P1 < 0.001 / P2 < 0.001 / P3 = 0.047
Six-minute walk test (meters), median (IQR)	360 (290–420)	440 (390–510)	390 (300–450)	420 (390–480)	P1 < 0.001 / P2 = 0.227 / P3 = 0.338
Six-minute walk test (% predicted), mean (SD)[b]	71.7 (23.6)	84.5 (20)	74.9 (23.9)	81.6 (19.2)	P1 = 0.005 / P2 = 0.363 / P3 = 0.284
Fatigue (Fatigue Severity Score ≥ 36) No. (%) of abnormal tests	16 (53%)	74 (33%)	13 (59%)	17 (27%)	P1 = 0.046 / P2 = 0.670 / P3 = 0.415
Fatigue Severity Score, median (IQR)	36 (22–49)	27 (14–41)	39 (26–51)	22 (13–39)	P1 = 0.046 / P2 = 0.670 / P3 = 0.415
Barthel Index, No. of patients (%)					P1 = 0.999 / P2 = 0.995 / P3 = 0.999
Totally Dependent (<20)	2 (7%)	0 (0%)	1 (5%)	0 (0%)	
Very Dependent (20–39)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	
Partially Dependent (40–49)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	
Minimally Dependent (60–79)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	
Independent (80–100)	25 (93%)	161 (100%)	19 (95%)	62 (100%)	

Abbreviations: ARDS: Acute Respiratory Distress Syndrome; CARDS: COVID-related Acute Respiratory Distress Syndrome; MRCss, Medical Research Council Sum Score.

[a] Calculated using established reference values provided by Gilbertson L et al. [12].

[b] Predicted value for the six-minute walk test was calculated according to Enright PL et al. [8].

[c] P1 = the significance of the measured variables in patients with CARDS compared to classic ARDS at 6 months. P2 = the significance of the difference between 6 months and 12 months in patients with classic ARDS. P3 = the significance of the interaction time and type of ARDS (CARDS vs Classical ARDS) at 6 months vs 12 months. The estimate difference between 6 months and 12 months for CARDS patients is presented in the text (Results) and **Supplementary Table 1**.

[d] Unknown or missing data (No. of missing patients, classic ARDS - CARDS): MRCss = 15–49 (6 months), 5–6 (12 months); hand grip strength = 17–33 (6 months), 5–5 (12 months); six-minute walk test = 24–62 (6 months), 12–6 (12 months); Fatigue Severity Score = 14–24 (6 months), 5–5 (12 months); Barthel Index = 17–87 (6 months), 7–5 (12 months).

CARDS at 6 months [7]. Hodgson et al. [10] and McPeake et al. [19] reported similar 6-month self-reported physical outcomes in classic ARDS and CARDS, but neither study performed any in-person strength evaluation.

Some study strengths and limitations should be considered in the interpretation of our results. The main strengths are: (1) the in-person follow-up evaluation of both cohorts of patients (CARDS and classic ARDS), including patients with CARDS during the first wave of the pandemic; and (2) the extensive physical examination carried out in our follow-up clinic, which included the MRC, hand grip dynamometry, and the 6MWT. Limitations of the study include the fact that patients with classic ARDS were provided by only one center (ASST Spedali Civili di Brescia); this could have introduced a selection bias for patients with classic ARDS. Moreover, patients were followed up for 1 year, but assessment at all time points was not possible in all patients due to time constriction at the moment of the paper's publication. Some potentially important confounders (vaccination status of COVID-19 patients and duration of NIV before starting mechanical ventilation) in the acute phase were not collected, and we did not calculate a priory the sample size, as we included all the patients available at the time of publication. Some patient-reported outcome measures, such as the FSS, are subject to patient recall bias. We did not analyze the diagnosis of ICU-acquired weakness, a potential contributor to poor long-term functional outcomes, neither at ICU nor at hospital discharge. We also had a certain amount of missing data that may limit the strength of our results. Finally, as an intrinsic limitation of an observational two-center study, the interpretation and the generalization of our results need to be confirmed in larger multicenter studies.

5. Conclusions

Both classic ARDS and CARDS survivors experienced long-term impairments in physical functioning, confirming that post-intensive care syndrome remains a major legacy of critical illness. Surprisingly, however, persisting disability was more common in survivors of classic ARDS than in CARDS survivors. In fact, muscle strength measured with HGD was reduced in survivors of classic ARDS compared to CARDS patients at both 6 and 12 months. The 6MWT was reduced and fatigue was more common in classic ARDS compared to CARDS at 6 months but differences were no longer significant at 12 months. Most patients in both groups regained independent function in ADLs at 6 months.

Author contributions

Simone Piva: Conceptualization, Methodology, Investigation, Data curation, Formal analysis, Writing – original draft, Writing – review & editing. Nicola Latronico: Conceptualization, Methodology, Writing – review & editing, Supervision. Francesco A. Rasulo: Conceptualization, Methodology, Writing – review & editing. Matteo Pozzi: Conceptualization, Methodology, Investigation, Data curation, Formal analysis, Writing – original draft, Writing – review & editing. Giacomo Bellani: Conceptualization, Methodology, Writing – review & editing. Giuseppe

Table 3
Adjusted analysis for physical performances and covariates during the acute phase of the ARDS for all the 296 patients included in the study.

	Dominant handgrip strength (Kg)		Dominant handgrip strength (% predicted)*		Six minutes walk test (meters)		Six minutes walk test (% Predicted)*		Fatigue (FSS ≥ 36)	
Predictors	*ED*	*p*	*ED*	*p*	*ED*	*p*	*ED*	*p*	*OR*	*p*
12 mo vs 6 mo in classic ARDS	3.98	**0.001**	9.73	**0.001**	32.45	0.234	6.01	0.278	1.28	0.720
CARDS vs Classic ARDS	12.70	**<0.001**	29.88	**<0.001**	90.23	**0.001**	10.91	**0.047**	0.22	**0.018**
Gender, Male	17.62	**<0.001**	11.48	**0.001**	77.50	**<0.001**	4.74	0.181	0.81	0.624
Age	−0.38	**<0.001**	−0.06	0.630	−2.53	**<0.001**	0.28	**0.024**	1.02	0.131
SAPS II	−0.03	0.608	0.02	0.873	0.40	0.446	0.01	0.924	1.02	0.141
Use of NIV pre-ICU admission	2.38	0.159	5.84	0.109	38.07	0.031	5.34	0.150	0.48	0.071
Prone position	2.72	0.063	3.03	0.333	7.53	0.621	1.54	0.626	1.14	0.720
Steroids in ICU	−0.97	0.529	−2.99	0.369	0.12	0.994	0.98	0.768	2.19	0.066
Use of vasopressor in ICU	−3.56	**0.013**	−6.39	0.038	13.68	0.352	1.10	0.723	0.58	0.137
ICU Length of stay	0.00	0.922	−0.08	0.134	−0.79	0.160	−0.06	0.594	1.01	0.232

List of abbreviations: ED, Estimate differences; OR, Odds ratio; ICU, Intensive Care Unit; CARDS, COVID19 related ARDS; SAPS II, Simplified Acute Physiology Score II; NIV, Non-Invasive Ventilation; LOS, Length of Stay.
* In these models Gender and age have not been included since the two variables are already included in the calculation of the dependent variables.

Foti: Conceptualization, Methodology, Writing – review & editing, Supervision. Alberto Goffi: Conceptualization, Methodology, Writing – review & editing. John C. Marshall: Conceptualization, Methodology, Writing – review & editing. Elena Peli: Investigation, Writing – review & editing. Nicola Gitti: Investigation, Writing – review & editing. Alberto Lucchini: Investigation, Writing – review & editing. Michele Bertoni: Investigation, Writing – review & editing. Stefano Calza: Formal analysis, Writing – review & editing. LOTO Investigators: Investigation, Writing – review & editing.

Ethics approval and consent to participate

The Provincial Ethics Committee of Brescia approved the study. Written informed consent was obtained from each participant at the time of the follow-up visit.

Founding source

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Declaration of Competing Interest

The authors declare no conflict of interest.

Data availability

The data described in this article can be accessed @ https://github.com/pivadoc/JCC/issues/new upon request.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.jcrc.2023.154285.

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