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ORIGINAL ARTICLE

One-year survival and Quality of Life of first wave COVID-19 invasively ventilated patients in Lombardy, Italy

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ABSTRACT

BACKGROUND: Lombardy was the epicenter of the first coronavirus disease 2019 (COVID-19) outbreak in western countries. The outbreak began in February 2020 and rapidly disseminated throughout the region. ICU beds were vastly insufficient and clinical knowledge of disease was poor at that time. Unfortunately, data on long-term mortality, morbidity, and Quality of Life are scarce and controversial. The aim of this study was to evaluate 1-year survival, Quality of Life, and functional recovery in patients with COVID-19 admitted to Intensive Care Units.

METHODS: All COVID-19 patients invasively ventilated and successfully discharged from 3 important academic hospitals in Lombardy were evaluated. Evaluations were performed by qualified medical staff and monitoring over time was performed by telephone call. Functional, cognitive, and psychological outcomes were explored using validated questionnaires. Selected patients were offered a follow-up chest computed tomography (CT) scan.

RESULTS: Four hundred twenty-seven patients were invasively ventilated and 268 (63%) were successfully discharged. Out of these 268 patients, 266 (99%) were alive at one year with no patient loss during follow-up. Very severe or severe dyspnea was reported by 7% of patients, while most patients (84%) did not experience dyspnea at rest. A small proportion of patients (17%) reported severe anxiety/depression. Good Quality of Life was reported by 64% of survivors. In patients complaining of dyspnea on exertion, fibrotic-like changes were observed at chest CT scans in 32/37 (86%) and 7/11 (63%) patients who underwent CT at 3 months and 1 year, respectively.

CONCLUSIONS: COVID-19 patients discharged from the hospital after invasive ventilation had excellent one-year survival and good overall recovery and Quality of Life.

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Lombardy was the first Italian region in Europe to be affected by the COVID-19 pandemic with a high number of infections, hospitalizations, and deaths. The fast progression of the disease in Lombardy served as a warning signal to other western countries around the world about the severity and rapid spread of SARS-CoV-2.[1] In Lombardy, the total Intensive Care Unit (ICU) capacity prior to the COVID-19 crisis was approximately 720 beds, which represented 2.9% of the total hospital capacity.[1] As of the end of March 2020, Lombardy ICU beds increased more than two folds and 1,324 beds were occupied by COVID-19 patients.[2] Still, facilities, healthcare workers and equipment were insufficient. Furthermore, an almost total lack of scientific evidence to provide adequate therapies for the management of COVID-19 patients led to a dramatic prognostic scenario, with higher than expected in-hospital mortality. Patients admitted to the ICU, particularly those requiring prolonged mechanical ventilation, often experience a variety of clinical, therapeutic, and emotional stressors resulting in physical, psychological, and cognitive impairments. This constellation of acquired disabilities is commonly referred to as Postintensive Care Syndrome. ICU survivors face a higher post discharge mortality and a lower Quality of Life, compared to a matched control group.[3] COVID-19 patients who required intensive medical treatments may develop pulmonary lesions other than multiple organ involvement driven by the virus' tropism for the cardiovascular, neurological, and musculoskeletal systems.[2] This multiorgan involvement may persist after recovery evolving into the so called long-COVID syndrome, which can occur in more than 10% of people infected with SARS-CoV-2.[4] However, data on follow-up of patients affected by severe COVID-19 disease requiring ICU admission during shortage of resources are scarce.[5, 6] In the hypothesis that COVID-19 could be associated with long-term mortality and poor Quality of Life, as in acute respiratory distress syndrome (ARDS) in settings with lack of resources, this study aimed to evaluate the one-year survival and Quality of Life of COVID-19 ICU patients who were invasively ventilated in three major academic hospitals in Lombardy during the first pandemic wave.

Materials and methods

Study design and setting

Consecutive patients with COVID-19 ARDS who received at least one day of invasive mechanical ventilation and were successfully discharged from three large academic hospitals in Lombardy, Italy, were followed up for one year.

Inclusion and exclusion criteria

We included all adult patients with SARS-CoV-2 infection confirmed by reverse transcriptase polymerase chain reaction (rt-PCR) based on nasal/oropharyngeal swab or bronchoalveolar lavage, that were admitted to the ICU and were invasively ventilated between February 24, 2020, and July 1, 2020, in three centers (Papa Giovanni XXIII Hospital, Bergamo, Italy; San Gerardo Hospital, Monza, Italy; IRCCS San Raffaele Hospital, Vita-Salute San Raffaele University, Milan, Italy). These centers were forced to rapidly increase their ICU bed capacity: from 28 to 72 ICU beds (54/72 dedicated to COVID patients) at San Raffaele Hospital, from 72 to 100 ICU beds (100/100 dedicated to COVID patients) at Papa Giovanni XXIII Hospital and from 31 to 97 ICU beds (84/97 dedicated to COVID patients) at San Gerardo Hospital. The ethical committee of each center approved the data collection.

Data collection

We collected baseline characteristics and number of comorbidities, ventilatory, hemodynamic and renal support, duration of invasive mechanical ventilation, length of ICU and hospital stay, and ICU and hospital mortality. Patients were routinely managed according to the guidelines available at that time, which included protective ventilation, pronation, and sedation, among others. The primary outcome was one-year survival. Trained investigators contacted discharged patients by phone at three, six, and 12 months. Patients were progressively registered in a dedicated database during the phone interview. If there was no response to the phone call, secondary telephone numbers or patients' general practitioners were contacted. If there was still no response, the database of the Lombardy re-

gion was used to determine patients' vital status. The follow-up started with the patient confirming their identity and date of birth, and then the investigators asked further contact details and information about working status at the onset of the disease (actively working or not), schooling (none, primary school, middle school, high school, Bachelor's Degree, Master's Degree), dysosmia and dysgeusia after discharge. Several tools were used to evaluate the physical, psychological, and cognitive aspects of Quality of Life. Heath-related Quality of Life was evaluated by European Quality of Life 5 Dimensions 3 Level Version (EQ-5D-3L) which included a self-assessment score and the Visual Analogue Scale (VAS). Psychological outcomes were evaluated using the Hospital Anxiety and Depression Scale (HADS), Post-traumatic stress disorder checklist for the DSM-5 (PCL-5) and Insomnia Severity Index (ISI). Cognitive status was assessed using the Italian telephonic version of the Mini Mental State Examination (MMSE). The presence of dyspnea at rest and on exertion was evaluated by Borg Category Ratio 10 Scale. Finally, nutritional status with the Mini Nutritional Assessment – Short Form (MNA-SF) and Functional Ambulation Classification (FAC) were used to assess nutritional status and walking independence. For patients with moderate or severe dyspnea on exertion, we offered a chest CT scan at three months and one year.

Statistical analysis

Data were presented as medians with interquartile range (IQR: 25th-75th percentiles) or as means with standard deviation (SD). Means and SD were used with normally distributed variables, while medians and IQR were used with non-normally distributed variables. Categorical and dichotomous variables were presented as absolute number and percentages. No data imputation for missing data was performed. A convenience sample was chosen for this observational study.

Results

Out of the 427 invasively ventilated patients with COVID-19 ARDS, 151 (35%) died in the ICU,

TABLE I.—*Baseline characteristics, clinical management, and complications of 268 COVID-19 ARDS patients who required invasive ventilation in the ICUs of three hospitals and were discharged home.*

Baseline characteristics	Value (N.=268)
Age (y), mean±SD	61±9
Male sex, N. (%)	205 (76)
BMI (kg/m^2), mean±SD	29±5
Comorbidities	
0, N. (%)	71 (30)
1, N. (%)	58 (24)
2, N. (%)	53 (22)
> 3, N. (%)	59 (24)
Schooling	
Middle school, N. (%)	76 (40)
High school, N. (%)	66 (35)
Bachelor's degree, N. (%)	48 (25)
Working status	
Working, N. (%)	133 (64)
Unemployed or retired, N. (%)	75 (36)
Management and complications	
Neuromuscular blocking agents, N. (%)	174 (73)
Prone positioning, no. (%)	185 (71)
Tracheostomy, N. (%)	74 (28)
ECMO, N. (%)	19 (7)
Inotropic support/vasopressors, N. (%)	106 (44)
CRRT, N. (%)	19 (7)
Days in hospital before ICU admission, median (IQR)	3 (1-5)
Length of mechanical ventilation, median (IQR)	13 (8-22.5)
Length of ICU stay, median (IQR)	16 (9-29.2)
Length of overall hospital stay, median (IQR)	40 (26-60)

ARDS: acute respiratory distress syndrome; BMI: Body Mass Index; CRRT: continuous renal-replacement therapy; ECMO: extracorporeal membrane oxygenation; ICU: Intensive Care Unit; IQR: interquartile range; PaO_2/FIO_2: arterial partial pressure of oxygen to fraction of inspired oxygen ratio; SD: standard deviation.

and 8 patients died before being discharged, accounting for a total of 159 (37%) in-hospital deaths. No patients were lost during the one-year follow-up, and two of them died during this timeframe. The two patients who died during the follow-up period after being discharged alive from the hospital (2/268, 0.7%) were a 72-year-old male, with systemic hypertension and obesity with previous history of myocardial infarction and thrombosis, and a 74-year-old female with chronic renal disease. The first patient died 4 days after being discharged, while the second died after 7 days. Table I provides the baseline characteristics and ICU management of the 268 survivors: patients were 61+ 9 years old, and the vast majority of them were male (205/268, 76%). They required a median of 16 (9 – 29) days in the ICU and 40 (26 – 60) hospital days before discharge. 174/268 (65%) patients received neuromuscular blocking agents and 185/268 (69%) were treated with prone position. Results of Quality of Life, psychological and cognitive outcome follow-up assessments are reported in Table II. Few patients reported alteration in taste or smell (7% and 9%, respectively) or being personally discriminated owing to the disease (3%). Quality of Life was generally good, and most o patients reported and upper (64%) or lower (17%) good recovery. Anxiety or depression were the most frequent severe complains and were reported by 17% of the in-

TABLE II.—*One-year functional outcomes of invasively ventilated COVID-19 ARDS survivors.*

	N. responders/N. of patients contacted	Value
Quality of Life		
Visual Analog Scale (VAS) for self-perceived health state, mean±SD	125/151	68 (±26)
EuroQol 5 Dimensions 3 Levels (EQ5D3L) – mobility	134/151	
No difficulty in walking, N. (%)		99 (74%)
Mild difficulty in walking, N. (%)		16 (12%)
Moderate difficulty in walking, N. (%)		9 (7%)
Cannot walk, N. (%)		3 (2%)
Unable to walk, N. (%)		7 (5%)
EuroQol 5 Dimensions 3 Levels (EQ5D3L) – self-care	133/151	
No difficulty in washing or dressing, N. (%)		117 (88%)
Mild difficulty in washing or dressing, N. (%)		11 (8%)
Moderate difficulty in washing or dressing, N. (%)		5 (4%)
EuroQol 5 Dimensions 3 Levels (EQ5D3L) – usual activities	133/151	
No difficulties in usual activities, N. (%)		105 (79%)
Mild difficulties in usual activities, N. (%)		14 (11%)
Moderate difficulties in usual activities, N. (%)		12 (9%)
Not able in usual activities, N. (%)		2 (2%)
EuroQol 5 Dimensions 3 Levels (EQ5D3L)—pain or discomfort	130/151	
No pain or discomfort, N. (%)		71 (55%)
Light pain/discomfort, N. (%)		36 (28%)
Moderate pain/discomfort, N. (%)		20 (15%)
High pain/discomfort, N. (%)		3 (2%)
EuroQol 5 Dimensions 3 Levels (EQ5D3L) – anxiety and depression	132/151	
Not anxious/depressed, N. (%)		80 (61%)
Moderately anxious/depressed, N. (%)		29 (22%)
Severely anxious/depressed, N. (%)		23 (17%)
Anxiety, depression, insomnia, and post-traumatic stress disorder		
Hospital Anxiety and Depression Scale (HADS) – anxiety, median (IQR)	132/151	3 (0-6)
Hospital Anxiety and Depression Scale (HADS) – depression, median (IQR)	132/151	2 (0-5)
Post-Traumatic Stress Disorder Checklist for DSM-5 (PCL-5), median (IQR)	130/151	20 (7-32)
Insomnia Severity Index (ISI), median (IQR)	133/151	1 (0-4)
Cognitive status		
Italian telephone Mini Mental State Examination (I-tel MMSE), median (IQR)	132/151	22 (22-22)
Additional Questions?		
Alteration in smell, N. (%)	130/151	12 (9%)
Alteration in taste, N. (%)	130/151	9 (7%)
Discrimination owing to the disease/personal – at least 1 episode, no (%)	130/151	4 (3%)
Discrimination owing to the disease/family – at least 1 episode, N. (%)	130/151	3 (2%)
Denied access to non-urgent care, N. (%)	130/151	2 (2%)

terviewed individuals. Regarding functional outcome (Table III), few patients reported severe or very severe dyspnea at rest (3% and 4%, respectively), malnourishment (5%), not being able to walk (2%) or needing continuous support while walking (5%). Fibrotic-like changes were observed in chest CT scans of 32/37 (86%) patients who rated their exertional dyspnea between 3 and 6 points of the Borg scale and accepted to perform the examination at three months and in 7/11 (63%) patients with similar symptoms at one year.

Discussion

Key findings

This multicenter study confirms that COVID-19 ARDS survivors who were invasively ventilated during the first pandemic wave in northern Italy experienced low mortality at one year, specifically 2/268 (0.7%). In addition, severe symptoms and poor Quality of Life were reported by ≤5% of patients, with the notable exceptions of severe anxiety or depression, which was instead observed in 17% of patients. Patients with persistent respiratory symptoms upon exertion had residual lung damage with pulmonary fibrotic-like changes.

Relationship to previous studies

Despite the ongoing debate, our data indicate that COVID-19 ARDS is slightly different from traditional ARDS, at least in long-term outcomes. Short term mortality in ARDS progressively declined over the last decades thanks to the improvement in ventilation strategies and ICU management, but still represents an important issue, with recent studies reporting in-hospital mortality ranging between 24% and 38%.[7, 8] In-

TABLE III.—*One-year functional outcomes of 151 invasively ventilated ICU patients with COVID-19 ARDS.*

Items	N. responders/N. of patients contacted	Values
Glasgow Outcome Scale extended (GOSe)	133/151	
Upper good recovery, N. (%)		85 (64%)
Lower good recovery, N. (%)		23 (17%)
Upper moderate disability, N. (%)		11 (8%)
Lower moderate disability, N. (%)		4 (3%)
Upper severe disability, N. (%)		5 (4%)
Lower severe disability, N. (%)		5 (4%)
Dyspnea at rest (Borg Category Ratio 10 scale)	134/151	
Nothing at all, N. (%)		112 (84%)
Light, N. (%)		5 (4%)
Moderate, N. (%)		8 (6%)
Strong, N. (%)		4 (3%)
Very strong, N. (%)		5 (4%)
Exertional dyspnea (Borg Category Ratio 10 scale)	134/151	
Nothing at all, N. (%)		47 (35%)
Very very slight, N. (%)		11 (8%)
Very slight, N. (%)		13 (10%)
Slight, N. (%)		17 (13%)
Moderate, N. (%)		26 (19%)
Somewhat intense, N. (%)		9 (7%)
Intense, N. (%)		4 (3%)
Severe, N. (%)		4 (3%)
Very severe, N. (%)		3 (2%)
Mini Nutritional Assessment–Short Form (MNA-SF)	133/151	
12-14 points (normal nutritional state), N. (%)		102 (77%)
8-11 points (at risk for malnutrition), N. (%)		24 (18%)
0-7 points (malnourished), N. (%)		7 (5%)
Functional Ambulation Classification (FAC)	132/151	
Can walk independently anywhere, N. (%)		106 (80%)
Requires help on stairs, slopes, or uneven surfaces, N. (%)		14 (11%)
Need continuous or intermittent support, N. (%)		4 (3%)
Need firm continuous support, N. (%)		6 (5%)
Cannot walk, N. (%)		2 (2%)

Percentages may not sum to 100 because of rounding.

hospital mortality in our population was 37%, which is in the upper range of that reported in traditional ARDS.[9] However, an important survival gap exists when considering the long-term outcome: <1% of our patients died after hospital discharge compared to the 10-20% observed in successfully discharged patients with non-COVID ARDS during the first year after discharge.[7, 8] A possible explanation is that patients included in this study belong to a more selected population compared to those included into previous, prepandemic, studies. COVID-19 patients, in particular those from the first pandemic wave, were not elders and had few comorbidities, and it can be speculated that this condition may be associated with better long-term survival. Moreover, the first wave of COVID-19 may have selected patients with a specific biologic background, more prone to positively react to the infection. The COVID-19 outbreak represented a stress-test for the health system worldwide. In Lombardy, due to the peculiar harshness of the pandemic, it could be hypothesized that some patients with a favorable biological profile had a better chance of surviving the acute phase of the infection and therefore surviving after the hospital discharge. In other words, an initial survival bias may have played a significant role, explaining the high survival rate we observed. We cannot definitely rule out which factors (either single or in combination) may contribute to this selection, but male gender, genetic profile, antibodies' glycosylation pattern, together with age and comorbidities have been linked to COVID-19 mortality and may explain the high survival rate of patients recovering from ICU and surviving the acute ARDS phase.[10-13] Relevant data on long-term Quality of Life and mortality after ARDS for COVID-19 infection are still scarce, but the high survival rate is not an isolated result. A recent paper reports that patients who received mechanical ventilation due to COVID-19 and were discharged from hospital had a 96% survival rate at the two-year follow-up, with no difference between patients who did and did not require invasive mechanical ventilation.[6] Pooling the initial experiences on long-term survival after COVID-19 allows, at least, to speculate that postdischarge mortality is lower than expected (despite the high mortality associated with the acute phase) and not related to the clinical severity of the indexed ICU admission. Nevertheless, our study is specifically focused on invasively mechanical ventilated patients during the first outbreak of COVID-19 pandemic. Patients and external conditions have been different during the various phases of the pandemic, mainly due to the development of effective vaccines and better knowledge about the disease thanks to the evidence generated during the various pandemic waves. It remains to be clarified whether vaccines and different subspecies of SARS-CoV-2 can influence Quality of Life and mortality after ICU stay. Few patients reported important reduction in their Quality of Life at one year after ICU discharge: a low percentage of patients complain dyspnea, malnourishment, or inability to walk. Reduction in physical function has already been reported at one year in COVID-19 ARDS survivors: a recent prospective multicenter study on 343 patients (Odissea Study) evaluated the health-related Quality of Life (HRQoL) 1 year after ICU stay, reporting that HRQoL in COVID-19 ARDS was reduced regarding the physical but not the mental component. However, a questionnaire testing the general impact on the mental and physical component was used in the study, with no detailing of specific symptoms.[14] The difference in applied test and outcome definition prevents us to make a direct comparison of this paper with our results. Invasively ventilated survivors in our study show a 7% incidence of severe or highly severe dyspnea at one year. Recent papers have reported the incidence of dyspnea ranging between 16% to 40%.[15] Methodologic discrepancies may explain this difference: most of authors used the modified Medical Research Council (mMRC) dyspnea scale while other studies only reported dyspnea presence or absence, without grading it. When comparing with severe dyspnea we are in line with previous findings (8%), confirming that long-term severe respiratory fatigue is rare, and patients survived to ICU tend to improve their respiratory function over one year after acute infection.[16] As for mortality, this data seem consistent over patients with different degrees of severity of the acute phase infection, since incidence

of dyspnea is similar between the general COVID-19 population and the specific subset of invasively ventilated patients. Similar findings were observed for pulmonary alterations at CT-scans: patients with persistent respiratory symptoms displayed altered CT-scan patterns, that tend to improve over the first year after discharge. Our results fit with those reported in the previous literature: fibrotic-like changes were observed in most patients (86%) with moderate-to-severe exertional dyspnea at three months in our population; such changes are reduced, but still relevant (63%) at one year. A recent metanalysis reports that ground-glass opacity and fibrotic-like changes were frequently observed in roughly 20% of patients, with a gradual recovery in the first year.[17] The higher incidence of CT abnormalities in our study is easily explained by the type of patients selected (*i.e.*, severe ARDS survivors mechanically ventilated in ICU). Our population is restricted to those patients having the highest degree of pulmonary injury, which has already been recognized as a risk factor for CT abnormalities.[17] Furthermore, chest CT scans in our study were limited to patients with moderate to severe dyspnea, thus more likely to have pulmonary abnormalities than those who were asymptomatic. Once combined, these factors may explain the higher incidence of fibrotic changes reported in our sample, but also add knowledge on the persistency of such changes in the specific population of invasively ventilated, ICU survivors (rather than in the general COVID-19 population). On the other hand, severe anxiety or depression were reported by 17% of patients as a significant long-term effect of SARS-CoV-2 infection. Our findings are in line with previous reports.[18] Nearly 20% of patients display anxious and depressive symptoms, and previous epidemics like severe acute respiratory syndrome (SARS) and Middle East Respiratory Syndrome (MERS) have already highlighted the distress associated with such situation. Our study confirms that one in five patients are likely to have mental sequelae after COVID-19 and this could be a long-term problem due to the impact on functional, social, and working ability of these individuals.[19] Malnutrition and sarcopenia have also emerged as a frequent issue in COVID-19 survivors, especially in the elderly and in ICU patients, because of the combination of the severe inflammatory processes, total or partial immobilization, and associated decline in functional status and anxiety/depression. A first survey showed that nutritional impairment of COVID-19 at hospital discharge is a risk for more than 80% of patients.[20] At six months postdischarge, 36% had persistent malnutrition, and 14.3% complained a significant decrease in muscle strength, with obese subjects and patients admitted to ICU having a higher risk of functional loss or undernutrition.[21] Data on long-term nutritional status in patients surviving ICU are scarce, but our study seems to reassure that most patients will return to their baseline one year after being discharged from the ICU. Indeed, according to the Mini Nutritional Assessment–Short Form at the 12-month follow-up, only 5% of our study population was malnourished. However, 18% have a concrete risk for altered nutritional status, confirming that nutrition should be carefully monitored in these patients and further studies are needed to clarify the long-term impact of COVID-19 (and specifically ICU stay) on such issue. Finally, most patients in our population completely recovered from any physical impairment. Other papers have already highlighted that a reduced physical and functional impairment exists in COVID-19 survivors at six months, especially after ICU admission.[22, 23] Data on long-term sequelae are scarce, however our results further reassure on this point: only a small percentage of patients still have difficulties in walking, carrying out daily activities and taking care of themselves, confirming the tendency to improve over the course of the first year.[23]

Implications of study findings

This study and the literature review indicate that patients with COVID-19-related ARDS have low mortality rates after ICU discharge and good overall long-term recovery. In general, the post-discharge data are reassuring for both physicians and patients. However, it is important to note that some patients may experience long-term respiratory complications, as evidenced by the fibrotic-like changes observed in the chest CT scans of a small proportion of patients in this study.

Limitations of the study

This study provides insight into the long-term outcomes of COVID-19-related ARDS in patients who were treated during the early stages of the pandemic. A strength of the study is that no patients were lost during follow-up, and there was almost complete questionnaire evaluation. Additionally, the authors used several previously validated scales to assess functional, psychological, and cognitive outcomes. The presence of quantitative radiologic data also represented a major strength of the study. However, the study had a relatively small sample size, and there was no control group (*i.e.*, non-COVID-19-related ARDS) or noninvasively ventilated patients included in the study, limiting the generalizability of the findings. Finally, our population may not be representative of the whole sample of Lombardy region during the first pandemic outbreak. Our study population consists of cases from three main academic hospitals which may have lower in-hospital mortality. However, regardless of in-hospital mortality and shortage of resources in the specific period of the first COVID-19 outbreak, our study demonstrates that the survival rate of invasively ventilated patients is high once they are discharged. In conclusion, considering both strengths and limitations, this study provides valuable insights into the long-term outcomes of COVID-19-related ARDS in patients who have received invasive mechanical ventilation. Further research is needed to understand the long-term outcomes of COVID-19 in a larger and more diverse patient population.

Future studies should aim to include a larger and more diverse patient population to confirm the low postdischarge mortality and good functional and radiologic recovery reported in this study. This will help to better understand the long-term outcomes of COVID-19-related ARDS and to improve patient care.

Conclusions

Despite the high rate of mortality in the ICU, COVID-19 patients discharged from the hospital after invasive ventilation had excellent one-year survival, which seems not to be associated with the clinical severity at ICU admission. Also, patients report good overall Quality of Life and effective recovery from any physical, radiologic, and functional impairment at one year after ICU admission, except for anxiety/depression that we confirm to be a significant long-term effect of COVID-19. Future studies should include a larger sample to confirm our data.

References

1. Grasselli G, Pesenti A, Cecconi M. Critical Care Utilization for the COVID-19 Outbreak in Lombardy, Italy: Early Experience and Forecast During an Emergency Response. JAMA 2020;323:1545–6.

2. Brandi N, Ciccarese F, Rimondi MR, Balacchi C, Modolon C, Sportoletti C, *et al.* An Imaging Overview of COVID-19 ARDS in ICU Patients and Its Complications: A Pictorial Review. Diagnostics (Basel) 2022;12:846.

3. Hill AD, Fowler RA, Pinto R, Herridge MS, Cuthbertson BH, Scales DC. Long-term outcomes and healthcare utilization following critical illness—a population-based study. Crit Care 2016;20:76.

4. Kenny G, Townsend L, Savinelli S, Mallon PW. Long COVID: clinical characteristics, proposed pathogenesis and potential therapeutic targets. Front Mol Biosci 2023;10:1157651.

5. Zangrillo A, Belletti A, Palumbo D, Calvi MR, Guzzo F, Fominskiy EV, *et al.*; COVID-BioB Study Group. One-Year Multidisciplinary Follow-Up of Patients With COVID-19 Requiring Invasive Mechanical Ventilation. J Cardiothorac Vasc Anesth 2022;36:1354–63.

6. Tresoldi M, Zangrillo A, Belletti A, Ramirez GA, Bozzolo E, Guzzo F, *et al.*; COVID-BioB Study Group. Two-year multidisciplinary follow-up of COVID-19 patients requiring invasive and noninvasive respiratory support. Minerva Med 2023. [[Epub ahead of print]]

7. Wang CY, Calfee CS, Paul DW, Janz DR, May AK, Zhuo H, *et al.* One-year mortality and predictors of death among hospital survivors of acute respiratory distress syndrome. Intensive Care Med 2014;40:388–96.

8. Sigurdsson MI, Sigvaldason K, Gunnarsson TS, Moller A, Sigurdsson GH. Acute respiratory distress syndrome: nationwide changes in incidence, treatment and mortality over 23 years. Acta Anaesthesiol Scand 2013;57:37–45.

9. Grasselli G, Greco M, Zanella A, Albano G, Antonelli M, Bellani G, *et al.*; COVID-19 Lombardy ICU Network. Risk Factors Associated With Mortality Among Patients With COVID-19 in Intensive Care Units in Lombardy, Italy. JAMA Intern Med 2020;180:1345–55.

10. White A, Kirby M. COVID-19: biological factors in men's vulnerability. Trends Urol Men's Health 2020;11:7–9a.

11. Velavan TP, Pallerla SR, Rüter J, Augustin Y, Kremsner PG, Krishna S, *et al.* Host genetic factors determining COVID-19 susceptibility and severity. EBioMedicine 2021;72:103629.

12. Xie Y, Butler M. Serum N-glycomic profiling may provide potential signatures for surveillance of COVID-19. Glycobiology 2022;32:871–85.

13. Petrović T, Alves I, Bugada D, Pascual J, Vučković F, Skelin A, *et al.* Composition of the immunoglobulin G glycome associates with the severity of COVID-19. Glycobiology 2021;31:372–7.

14. Deana C, Vetrugno L, Cortegiani A, Mongodi S, Salve G, Mangiagalli M, *et al.*; On Behalf Of The Italian Odissea Group. Quality of Life in COVID-Related ARDS Patients One Year after Intensive Care Discharge (Odissea Study): A Multicenter Observational Study. J Clin Med 2023;12:12.

15. Lerum TV, Meltzer C, Rodriguez JR, Aaløkken TM, Brønstad E, Aarli BB, *et al.* A prospective study of pulmonary outcomes and chest computed tomography in the first year after COVID-19. ERJ Open Res 2023;9:00575-2022.

16. Lorent N, Vande Weygaerde Y, Claeys E, Guler Caamano Fajardo I, De Vos N, De Wever W, *et al.* Prospective longitudinal evaluation of hospitalised COVID-19 survivors 3 and 12 months after discharge. ERJ Open Res 2022;8:00004-2022.

17. Watanabe A, So M, Iwagami M, Fukunaga K, Takagi H, Kabata H, *et al.* One-year follow-up CT findings in COVID-19 patients: A systematic review and meta-analysis. Respirology 2022;27:605–16.

18. Khraisat B, Toubasi A, AlZoubi L, Al-Sayegh T, Mansour A. Meta-analysis of prevalence: the psychological sequelae among COVID-19 survivors. Int J Psychiatry Clin Pract 2022;26:234–43.

19. O'Brien K, Townsend L, Dowds J, Bannan C, Nadarajan P, Kent B, *et al.* 1-year quality of life and health-outcomes in patients hospitalised with COVID-19: a longitudinal cohort study. Respir Res 2022;23:115.

20. Cuerda C, Sánchez López I, Gil Martínez C, Merino Viveros M, Velasco C, Cevallos Peñafiel V, *et al.*; NUTRICOVID study research group of SENDIMAD. Impact of COVID-19 in nutritional and functional status of survivors admitted in intensive care units during the first outbreak. Preliminary results of the NUTRICOVID study. Clin Nutr 2022;41:2934–9.

21. Gérard M, Mahmutovic M, Malgras A, Michot N, Scheyer N, Jaussaud R, *et al.* Long-Term Evolution of Malnutrition and Loss of Muscle Strength after COVID-19: A Major and Neglected Component of Long COVID-19. Nutrients 2021;13:3964.

22. Baricich A, Borg MB, Cuneo D, Cadario E, Azzolina D, Balbo PE, *et al.*; No-more Covid Group. Midterm functional sequelae and implications in rehabilitation after COVID-19: a cross-sectional study. Eur J Phys Rehabil Med 2021;57:199–207.

23. Carenzo L, Protti A, Dalla Corte F, Aceto R, Iapichino G, Milani A, *et al.*; Humanitas COVID-19 Task Force. Short-term health-related quality of life, physical function and psychological consequences of severe COVID-19. Ann Intensive Care 2021;11:91.

Conflicts of interest
The authors certify that there is no conflict of interest with any financial organization regarding the material discussed in the manuscript.

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Authors' contributions
Luca Lorini, Giuseppe Foti and Giovanni Landoni have given substantial contributions to the study conception, design and supervision; Rosa Labanca, Luca Lorini, Giuseppe Foti and Giovanni Landoni contributed to the project administration and to the study validation; Rosa Labanca, Dario Bugada, Sara Cazzaniga, Filippo D'Amico, Lorenzo Grazioli, Marilena Marmiere, Luca Novelli, Matteo Pozzi, Roberto Rona, Marco Giani, Valeria Bellin, Alberto Lucchini, Federico Raimondi, Margherita Rocchi and Maria T. Salvioni contributed to the data collection; Rosa Labanca contributed to the data analysis; Rosa Labanca, Dario Bugada, Luca Novelli, Matteo Pozzi and Federico Raimondi contributed to the data interpretation; all authors equally contributed to the manuscript draft, revision and editing. All authors read and approved the final version of the manuscript.

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