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## Letter to the Editor

## Management and outcomes of post-acute COVID-19 patients in Northern Italy



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## Dear Editor

Italy is one of the most affected countries by COVID-19 pandemic which has led to dramatic effects throughout the world with millions infected people and hundreds thousand deaths. The disease can cause major alveolar damage resulting in hypoxemic acute respiratory failure (ARF), needing admission to intensive care units (ICU), continuous positive airway pressure (CPAP), non-invasive ventilation (NIV) or invasive mechanical ventilation (IMV) in a high proportion of cases [1]. Preliminary information is available in critical patients, whereas less has been reported on interventions and outcomes after the acute phase.

The Italian regions Lombardy and Piedmont have the highest prevalence of infected people (more than 105,000 reported cases out of 14,500,000 inhabitants) resulting in shortage of ICU beds [2]. To free up beds in the acute care hospitals, patients with COVID-19 associated to *de novo* ARF, no longer requiring ICU, but still too unstable to be discharged home, were transferred to the Istituti Clinici Scientifici (ICS) Maugeri network, a multicentre referral Institution for pulmonary rehabilitation and chronic care [3]. We report the management and outcomes of patients with nasal/throat swabs still positive for SARS-CoV-2 by polymerase chain reaction, admitted to five centres (Lumezzane, Pavia, Veruno, Montescano, Tradate) of the network between March, 10th and April, 30th.

An *ad hoc* task force organised the hospital structures and activities to face this emergency. In and outpatient rehabilitation programs for stable non COVID-19 patients were stopped, patients discharged, and scheduled admissions delayed. A multidisciplinary team developed algorithms to drive the clinical activities in the wards. Effective protective personal equipment such as masks, N95/FFP2 respirators, gowns hair covers, gloves, eye and face shields were provided to all professionals in all occasions [4].

In addition to respiratory therapy, according to the evolving information and current research [5], one or more of the following drugs were added as specific therapy for COVID-19: chloroquine, antiviral, steroids, and anticoagulants. Patients underwent also the therapy for their underlying comorbidities [5]. Respiratory (i.e., protocols dedicated to pronation, oxygen and ventilators use) and motor physiotherapy sessions (reconditioning and physical activity as arm and/or leg cranks, low intensity aerobic exercises, walking at light-to-moderate intensity) were also proposed for at least 20 min a day [6].

In the period under observation 907 patients were admitted and 553

of them (60.9%) were discharged. According to this definite outcome, discharged patients were considered as “ended cases” and divided in two groups: those recovered and discharged home (recovered) and those transferred to acute care hospitals or died (failure), whose data were analysed together. Results are shown in Table 1.

The majority of patients were males older than sixty years, with more than one comorbidity, the failure group being older and with more comorbidities.

These patients were still severe as shown by the high proportion of them needing oxygen, high flow nasal cannula (HFNC) or ventilatory support, by the high treatment failure requiring transferral to acute care hospitals, and high mortality rate. Indeed, out of 553 discharged cases at the end of observation, 82.1% were considered as recovered and discharged home, whereas 17.9% were either transferred to acute care hospitals (5.8%) or died (12.1%). Patients discharged home from two centres underwent a telemedicine program consisting of pulse oximetry monitoring and telenursing, telerehabilitation and second opinion consultation.

High mortality rates are reported for patients with SARS-CoV-2 admitted to ICU [1]. This is one of the first reports on the outcomes of post-acute COVID-19 patients and the high mortality rate indicates that even when patients are discharged from acute care hospitals, their conditions may still be severe and require monitoring and complex interventions. Patients of two groups required oxygen supplementation in a similar proportion, whereas died and transferred patients required more non-invasive ventilator support. Guidelines give indications regarding the use of non-invasive ventilatory support to avoid IMV, with some advocating HFNC over NIV or vice versa [7,8]. There have been no randomized control trials on the use of either HFNC or NIV in coronavirus-related pneumonia to avoid intubation, and even less information is reported on the use of these tools after the acute phase. This issue is particularly important as all modalities of non-invasive ventilatory support or even simple oxygen supplementation via cannula can be a source of aerosol contamination [9]. Recently, in these patients it has been proposed to add prone position while performing NIV [10].

Our patients underwent also medical therapy with drugs claimed, but not proven, to be successful for treating COVID-19. Despite patients did not complain any adverse effect, at present no drug has been approved or proven to be safe and effective to treat these patients. Definitive clinical trials are needed to identify optimal treatments [5].

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**Table 1**

Demographic, clinical characteristics, hospital history, interventions required by and outcome of 553 closed cases. Data as mean ± Standard Deviation, or numbers (%).

	Recovered	Failure	P value
Patients, n (% of discharged cases)	454 (82.1)	99 (17.9)	0.001
Transferred to acute care hospitals, n (%)	—	32 (5.8)	—
Died patients, n (%)	—	67 (12.1)	—
Age, years	69.1 ± 14.2	78.2 ± 11.2	0.001
Patients younger than 60 years, n (%)	136 (29.9)	2 (2.0)	0.001
Male, n (%)	276 (60.8)	69 (69.7)	0.0935
Comorbidities per patient, n	1.9 ± 1.6	3.3 ± 2.2	0.001
<b>Referring hospitals</b>			
Symptom onset, days	6.0 ± 3.4	7.1 ± 3.1	0.0032
LOS, days	12.8 ± 9.3	13.9 ± 10.3	0.2963
Patients on CPAP or NIV, n (%)	78 (17.2)	20 (20.2)	0.4770
Patients on IMV, n (%)	25 (5.5)	8 (8.1)	0.3406
Tracheostomized in SB, n (%)	12 (2.6)	1 (1.0)	0.3373
Tracheostomized under IMV, n (%)	9 (1.9)	0 (0.0)	0.1669
<b>ICS network</b>			
LOS, days	20.2 ± 13.3	18.3 ± 18.4	0.1990
Patients under O <sub>2</sub> therapy only, n (%)	290 (63.9)	74 (74.7)	0.0363
Maximal FiO <sub>2</sub> used, (%)	0.29 ± 0.12	0.60 ± 0.11	0.001
Patients on O <sub>2</sub> + HFNC, n (%)	11 (2.4)	6 (6.0)	0.0589
Patients on O <sub>2</sub> + CPAP or NIV, n (%)	36 (7.9)	33 (33.3)	0.001
CPAP/NIV failure rate, n (%)	0 (0.0)	18 (54.5)	0.001
Discharged to telenursing, n (%)	93 (20.4)	—	—

Abbreviations: CPAP: continuous positive airway pressure; FiO<sub>2</sub>: inspiratory oxygen fraction; HFNC: high flow nasal cannula; ICS: Istituti Clinici Scientifici; IMV: invasive mechanical ventilation; LOS: length of stay; NIV: non-invasive ventilation; SB: Spontaneous breathing. Statistical methods: for continuous variable unpaired t-test and for % proportion test were conducted.

Our patients underwent also short sessions of reconditioning and physiotherapy. Despite fatigue is a highly prevalent symptom in patients with COVID-19 infection and most of the hospitalized COVID-19 patients have a prolonged length of stay in ward, the effect of muscle activity in the course of viral infections is unknown. Many countries have had a complete lockdown, preventing participation in regular rehabilitation programs in most outpatient centers and/or the delivery of home programs or other individualized treatments. Telemedicine can be a useful tool to obviate this problem, however, only one fifth of discharged patients could undergo such modality.

What lesson can we learn? The pathophysiology of COVID-19 inducing ARF requires high skill by physicians and other professionals. Besides providing the proper safety equipment, an appropriate use of available technologies is required. Robots, Artificial Intelligence, Big Data Analytics, mobile apps and telemedicine will be effective resources in fighting pandemic [11].

In conclusion, this letter provides characteristics and outcomes of post-acute patients with confirmed COVID-19 in Northern Italy. These patients are still a challenge for the health system due to high need of monitoring, complex respiratory support, high risk of further decompensation and death.

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## Declaration of Competing Interests

Authors do not report any conflict of interest.

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