Finally, regardless of their respiratory support patients who are admitted to hospital from home with suspicion of having COVID-19–associated respiratory failure, should be closely monitored for deterioration. An emergency care pathway including an escalation plan and ceiling of care should be discussed and documented on arrival.

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Functional impairment during post-acute COVID-19 phase: Preliminary finding in 56 patients

Dear Editor,

Rehabilitation in a bedded setting is estimated to be needed in 4% of 2019 novel Coronavirus (COVID-19) patients discharged from hospital, especially from Intensive Care Unit (ICU).[1]

Functional impairment of patients surviving the COVID-19 acute phase has been poorly described, and the only available information is provided by experts[2] or inferred from patients with other clinical conditions (e.g., Acute Respiratory Failure-ARF).[3] Two recent studies suggested that early, post-hospitalization rehabilitative interventions would be recommended.[4,5]

Aim of this study is to assess the clinical and functional presentation of post-acute COVID-19 patients at admission for inpatient rehabilitation. All consecutive COVID-19 patients admitted to undergo inpatient rehabilitation at Isti-

tuti Clinici Scientifici (ICS) Maugeri, Tradate, Italy between April 1st and July 31st were evaluated. The study was approved by the Central Ethical Committee of ICS Maugeri (CEC2279; March 12th, 2020) and patients signed the consent form. Healthcare operators were trained in personal protection measures.[6] The following evaluations were performed: clinical examination (including vital signs and blood gas analysis) and anthropometric assessment. Dyspnoea and perceived health state were measured by Barthel Dyspnea Index (Bd) (total scores range from 0-best- to 100-worst-), and Euro Quality of Life (EuroQoL-VAS), respectively (total scores range from 0-worst- to 100-best-), whereas disability with Barthel Index (Bi) (total scores range from 0-worst- to 100-best-), and Short Physical Performance Battery (SPPB) (total score results from the sum of three scores: standing balance, walking, and standing from sitting position, with disability if <9—1/2: severe; 3/8 moderate-).[7] Functional assessment with Medical Research Council Muscle (MRCm) strength test for quadriceps and biceps (≥4 normal) and respiratory muscles fatigue with Single Breath Counting (SBC) were also evaluated.

Exercise capacity was assessed with the 6-min walk test (6MWT) or One Minute Sit to Stand (1STS)[8] (reference value of repetitions: 30–37/min in men and 27–34/min in women, aged 60–79 years). Data accounted for length of stay (LoS) before admission for pulmonary rehabilitation, previous treatment for ARF (Invasive Mechanical Ventilation (IMV), Non-Invasive mechanical Ventilation (NIV), and oxygen), comorbidities (Cumulative Illness Rating Scale (CIRS)) gender and age.

Table 1 Baseline characteristics of 56 patients surviving the acute COVID-19 phase.

	All	IMV (n = 24)	NIV (n = 11)	Oxygen (n = 21)	p-Value
Males, n (%)	39 (69.6)	19 (79.2)	7 (63.6)	13 (61.9)	0.40
Age, years	69.4 (9.9)	64.5 (8.7)	71.6 (7.6)	73.8 (10.2)	0.004[b]
LoS, days	48.0 (17.4)	57.9 (14.2)	42.5 (15.5)	39.4 (16.4)	0.0004[c]
BMI, kg/m^2	25.3 (23.2–27.4)	24.9 (23.2–28.9)	23.9 (20.4–30.1)	25.6 (23.9–27.3)	0.67
FiO_2	0.21 (0.21–0.24)	0.21 (0.21–0.21)	0.21 (0.21–0.28)	0.21 (0.21–0.21)	0.24
PaO_2, mmHg	82.4 (73.3–95.4)	83.3 (74.2–100.5)	79 (67–92.9)	84.4 (76.5–93.4)	0.73
$PaCO_2$, mmHg	34.1 (32.4–38.3)	32.8 (31.6–35.1)	33.4 (32.3–38.4)	34.7 (33.4–39.6	0.05
pH	7.44 (7.42–7.45)	7.431 (7.42–7.456)	7.44 (7.40–7.46)	7.439 (7.406–7.447)	0.61
CIRS CI	1.7 (0.3)	1.6 (0.2)	1.7 (0.3)	1.7 (0.3)	0.81
CIRS SI	3.4 (1.5)	3.3 (1.2)	3.6 (1.5)	3.6 (1.8)	0.74
Bi	68.7 (28.0)	62.6 (26.3)	74.3 (25.9)	74.7 (30.9)	0.39
Bd	20 (11–40)	26.5 (12.5–46.5)	22 (17–34)	13 (9–27)	0.21
SBC	20.4 (10.6)	20.5 (10.7)	17 (8.4)	22.9 (11.9)	0.46
SPPB total score	0.5 (0–6)	0 (0–5)	0 (0–6)	2 (0–8)	0.34
SPPB balance testing	1.6 (1.8)	1.5 (1.8)	1.7 (2.0)	1.5 (1.6)	0.94
SPPB walk	0 (0–3)	0 (0–2)	0 (0–3)	1 (0–3)	0.55
SPPB stands	0 (0–1)	0 (0–1)	0 (0–1)	0 (0—1)	0.55
MRC Quadriceps	3.9 (0.9)	3.9 (0.9)	4.3 (0.8)	3.7 (0.8)	0.34
MRC Biceps	4.1 (0.8)	4.2 (0.8)	4.2 (1.0)	3.9 (0.8)	0.53
1STS, number of stands	0 (0—10)	0 (0—0)	0 (0—9)	9 (0—17)	0.006[d]
6MWT, meters	0 (0—0)	0 (0—0)	0 (0—0)	0 (0—0)	0.84
EuroQoL-VAS	60.6 (19.1)	54.8 (17.6)	68.6 (21.5)	63.0 (18.2)	0.10
Deviation from normal value[a]					
σ SPPB total score (n = 50)	9 (4—9)	9 (5—9)	9 (4—9)	8 (5—9)	0.81
σ 1STS, number of stands	33 (23.5—35.0)	35 (34–35)	33(26–35)	25 (16–35)	0.002[e]
σ 6MWT, meters	482 (419—539)	515.5 (464.5–568.5)	483 (383–537)	457 (369–481)	0.004[f]
σ SBC (n = 21)	7.9 (5.3)	7.3 (5.8)	8.7 (4.8)	7.8 (5.7)	0.90
σ MRCm Quadriceps (n = 15)	1	1	1	1	–
σ MRCm Biceps	1	1	1	1	–

Value are expressed as number, mean or median SD or IQR.
Legend: IMV: Invasive Mechanical Ventilation; NIV: Non Invasive Mechanical Ventilation; LoS: length of stay; BMI: body mass index; FiO_2: fraction of inspired oxygen; PaO_2: partial pressure of oxygen; $PaCO_2$: partial pressure of carbon dioxide; CIRS: Cumulative Illness Rating Scale including the comorbidity index (CI) and the severity index (SI); Bi: Barthel of activity of daily life; Bd: Bathel dyspnoea; SBC: Single Breath Counting; SPPB: Short Physical Performance Battery; MRCm: Medical Research Council Muscular; 1STS: One Minute Sit to Stand; 6MWT: six minute walk test; EuroQoL-VAS: Euro Quality of Life with visual analogue scale. Sidak and Bonferroni multiple comparison tests were performed.

[a] Estimation of variability of the outcome in relation to reference values.
[b] IMV VS. Oxygen p-value = 0.004.
[c] IMV VS. Oxygen p-value = 0.02; IMV VS. Oxygen p-value = 0.001.
[d] IMV VS. Oxygen p-value = 0.002.
[e] IMV VS. Oxygen p-value = 0.0008.
[f] MV VS. Oxygen p-value = 0.004.

Table 2 Correlations between LoS, age, CIRS and impairment outcomes.

	LoS Rho (p-value)	Age Rho (p-value)	CIRS CI Rho (p-value)	CIRS SI Rho (p-value)
Bi	−0.47 (0.002)	−0.21 (0.19)	−0.10 (0.53)	−0.08 (0.60)
Bd	0.37 (0.008)	0.14 (0.32)	0.12 (0.41)	0.11 (0.42)
SBC	−0.38 (0.03)	−0.13 (0.45)	0.05 (0.81)	0.04 (0.83)
SPPB TOT	−0.12 (0.38)	−0.02 (0.91)	0.05 (0.74)	0.03 (0.82)
MRCm Quadriceps	0.25 (0.15)	−0.46 (0.004)	−0.14 (0.42)	−0.16 (0.35)
MRCm Biceps	0.28 (0.10)	−0.21 (0.20)	−0.05 (0.76)	−0.12 (0.48)
1STS	−0.34 (0.18)	−0.04 (0.86)	0.06 (0.81)	−0.05 (0.83)
6MWT	–	−0.74 (0.47)	0.92 (0.26)	0.95 (0.20)
EuroQoL-VAS	−0.31 (0.04)	0.05 (0.75)	0.11 (0.46)	0.02 (0.89)

Legend: LoS: length of stay; CIRS: Cumulative Illness Rating Scale including the comorbidity index (CI) and the severity index (SI); Bi: Barthel of activity of daily life; Bd: Bathel dyspnoea; SBC: Single Breath Counting; SPPB: Short Physical Performance Battery; MRCm: Medical Research Council Muscular; 1STS: One Minute Sit to Stand; 6MWT: six minute walk test; EuroQoL-VAS: Euro Quality of Life with visual analogue scale.

Qualitative and quantitative variables were described with absolute and relative (percentage) frequencies and means (standard deviations, SD) or medians (interquartile ranges, IQR), depending on their normal or non-normal distribution, respectively. Demographic, epidemiological, and clinical variables were compared, stratifying by ICU stay and gender. Chi-squared or Fisher exact test was used for qualitative variables; analysis of variance or Kruskall–Wallis was computed for quantitative variables with a normal or non-normal distribution, respectively. CIRS and LoS were correlated with key clinical variables (Spearman's correlation) and were ranked according to the Chan's classification. A p-value <0.05 was considered statistically significant.

All 56 patients showed a reduced Bi and EuroQoL-VAS and increased Bd (Table 1). Overall 27/56 (48.2%) patients had a total SPPB score of 0, 22/56 (39.3%) between 1 and 8, and 7/56 (12,5%) ≥9. The SPBB 'standing balance' was less than 4 in 40 (71.4%) patients. Only 19/56 (33.9%) completed the 1STS test with a median (IQR) number of 14 (9.3–19.8) repetitions. The majority (53, 94.6%) could not perform the 6MWT and 5.4% covered a mean (SD) distance of 423.7 (34.8) m, around 70% of the Enright predicted value.

No statistically significant differences were found for clinical and functional data between males and females.

Patients previously treated with IMV were younger (p-value: 0.004), experienced a longer LoS (p-value: 0.0004), and had worse 1STS (p-value: 0.006) when compared with patients previously treated with oxygen (Table 2).

Furthermore, a statistically significant fair correlation was found between LoS and Bi, Bd, SBC and EuroQoL-VAS and between age and MRC quadriceps oriented to a worse functional and symptomatic status.

The results of the present study show that COVID-19 survivors can have an impairment of functional and muscular performance, dyspnoea, as well as impaired perceived health state. Patients who underwent IMV were younger, had a longer LoS and could not perform any exercise test.

Our patients, without acute respiratory failure, showed more clinical complications (*i.e.*, reduced ability to carry out daily living activities and moderate dyspnoea, even at rest) when compared with another cohort, which included respiratory failure survivors with an average SPBB < 4.[9]

Our findings are consistent with those of recent studies,[4,5] where post-acute COVID-19 patients suffer from dyspnoeaand severe disability. Although information about fatigue is missing in our study; a recent review underlined this as an important outcome in pulmonary rehabilitation.[10] These data support the rationale for pulmonary rehabilitation, being effective in reducing dyspnea and fatigue, improving exercise capacity and quality of life.

In conclusion, our preliminary data suggest indication for previously hospitalized COVID-19 patients to undergo a comprehensive clinical and functional assessment to identify those who are likely to benefit from rehabilitation. However, future studies in this field are also needed about potential effects of pulmonary rehabilitation.

Conflicts of interest

The authors have no conflicts of interest to declare.

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Non-invasive ventilation through a nasal interface during transoesophageal echocardiogram in a high-risk chronic patient

Dear Editor,

Non-invasive ventilation (NIV) has been an efficient strategy for ventilatory support and sedation related respiratory failure prevention during endoscopic procedures in high-risk patients. However, there is not enough evidence concerning the ideal pressure setting and choice of interface, mainly in home mechanical ventilated patients that have different interface options.[1]

We report the use of NIV in a high-risk chronic patient undergoing transoesophageal echocardiography (TEE) under sedation using her own home care vented nasal interface with intentional leaks (Mirage FX™, ResMed, Australia).

The patient was a 31-year-old woman, 45 kg weight, with a previous medical history of cystic fibrosis, chronic respiratory failure and end-stage kidney disease. She was on home mechanical ventilation with high ventilatory dependency (>18 h/day) in spontaneous/timed (ST) bi-level pressure cycled mode [inspiratory positive airway pressure (IPAP) of 17 cmH_2O; expiratory positive airway pressure (EPAP) of 4 cmH_2O; backup respiratory rate (RR) of 16 cpm], alternating between oro-nasal and nasal interface during sleep and daytime, respectively, continuous oxygen (O_2) therapy (2 L/min) and haemodialysis through a catheter placed in the right atrium.

She was hospital admitted due to fluid overload and fever of unknown origin. Aetiological investigation isolated a *Methicillin-susceptible Staphylococcus aureus* in blood cultures without evidence of respiratory or urinary tract infection. Transthoracic echocardiogram showed a mass in the right atrium in relation to the catheter, requiring TEE characterisation.

Monitoring during TEE included non-invasive blood pressure and pulse oximetry (SpO_2). NIV was applied with ST bi-level pressure cycled mode using an acute hospital ventilator with an O_2 blender permitting a fraction of inspired oxygen (FiO_2) of 100% (*Trilogy 202™, Philips Respironics, Pennsylvania, United States*). The interface was patient's home care vented nasal mask. Sedation was performed with intravenous midazolam — intended sedation level of -3 in the Richmond Agitation Sedation Scale (RASS).