

Respiratory rehabilitation for patients with COVID-19 infection and chronic respiratory failure: a real-life retrospective study by a Lombard network

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Abstract

The Lombardy region has been one of the areas most affected by the COVID-19 pandemic since the first months of 2020, providing real-life experiences in the acute phase. It is unclear how the respiratory rehabilitation network responded to this emergency. The aims of this retrospective study were: i) to analyze clinical, functional, and disability data at admission; ii) describe assessment tools and rehabilitative programs; iii) evaluate improvement after rehabilitation. The study was conducted on data collected from ten pulmonary rehabilitation centers in Lombardy, between the period of March 1st 2020 to March 1st 2021, in patients with respiratory failure recovering from COVID-19 both at admission and discharge. The study included demographics, comorbidities, nutritional status, risk of falls, disability status (Barthel index; Short Physical Performance Battery (SPPB); 6 minutes walking test (6MWT), symptoms (dyspnoea with Barthel Dyspnoea and MRC Dyspnoea Scale), length of stay, discharge destination, need for mechanical ventilation, respiratory function, assessment/outcomes indices, and prescribed rehabilitative programs. 413 patients were analyzed. Length of stay in acute and rehabilitative units was less than 30 days. Fifty % of patients used non-invasive ventilation during their stay. Functional status was mildly compromised for forced volumes and oxygenation, while severely compromised for diffusion capacity. Independency was low while physical performance status very low. At discharge, 318 (77%) patients were sent home, 83 (20.1%) were transferred to an acute unit and 12 (2.9%) passed away. Barthel Index and 6MWT were the most used tests, while MRC score was the least used outcome parameter. The 5 main rehabilitative activities were walking (90.8%), transfer from bed to armchair (77.5%), limb mobilization in bed (76%), balance (71.2%), and cycle-ergometer or treadmill (43.1%). A huge difference was found in admission, discharge, and delta change among different rehabilitative centers. When available, all outcomes showed a significant improvement. With the limitation of a retrospective study with a clear amount of missing data, COVID-19 subjects admitted to rehabilitative centers presented a reduced physical performance, symptoms of dyspnoea, and severe disability. The 6MWT and Barthel index were the most used measurement.

Introduction

The pulmonary disease developed by subjects infected with COVID-19 virus proved to be extremely heterogeneous in terms of clinical presentation, disability, outcomes and prognosis [1-3]. The possible outcomes after hospitalization are residual symptomatic limitations, functional damage, the appearance of disability, reduced exercise tolerance and neuropsychological damage [1-3]. Panels of experts have proposed rehabilitation paths [4-6] and some scientific reports have already highlighted the benefits of post-COVID-19 pneumonia rehabilitation programs [7-9]. In Lombardy (the most populated Italian region with more than 10 million residents) there are plenty of pulmonary rehabilitation opportunities, but they vary in volume of activities after acute hospitalisation. During the first months of 2020, Lombardy has been one of the areas most affected by the COVID-19 pandemic, providing real life experiences both in the post-acute phase [10] and in rehabilitation [7, 8]. It is unclear how the respiratory rehabilitation network responded to this emergency. To help clarify this, three scientific respiratory societies - ARIR (Associazione Riabilitatori dell'Insufficienza Respiratoria), AIPO (Associazione Italiana Pneumologi Ospedalieri) and SIP (Società Italiana di Pneumologia) - have proposed a "real-life" evaluation that investigates activities dedicated to post-COVID-19 patients.

The aims of this retrospective study were to: i) analyse clinical, functional and disability data at admission; ii) describe the measurement tools and the proposed rehabilitative program; iii) evaluate improvement after rehabilitation for patients with respiratory failure as a consequence of SARS-CoV-2 pneumonia.

Ethical statement

The study was approved by the Istituti Clinici Scientifici (ICS) Maugeri Ethics Committee (CEC 2279; March 12th, 2020). At admission to institutions, patients gave informed consent for the scientific use of their data. As retrospective analysis, the study was not registered.

Patients

This study was conducted on the Automated Integrated Health Care Records databases on available data collected from ten pulmonary rehabilitation centres in Lombardy: ICS Maugeri Hospitals (Lumezzane, Tradate, Pavia, Montescano, Milan); Sant'Antonio Abate Hospital, Cantù; San Giuseppe Hospital, Milan; Santa Marta Hospital, Rivolta d'Adda; Casa di Cura Ancelle della Carità, Cremona and Brescia; Fondazione Teresa Camplani (FTC), Cremona and Brescia (Figure 1).

The study period was from March 1st 2020 to March 1st 2021. Included patients were recovering from pneumonia related to COVID-19 and consecutively admitted for inpatient pulmonary rehabilitation. Concerning provenience, these patients came from intensive and sub-intensive care units, general wards or home. They required oxygen supply, non-invasive ventilation (NIV) or invasive mechanical ventilation (IMV) [11,12]. There were no specific exclusion criteria.

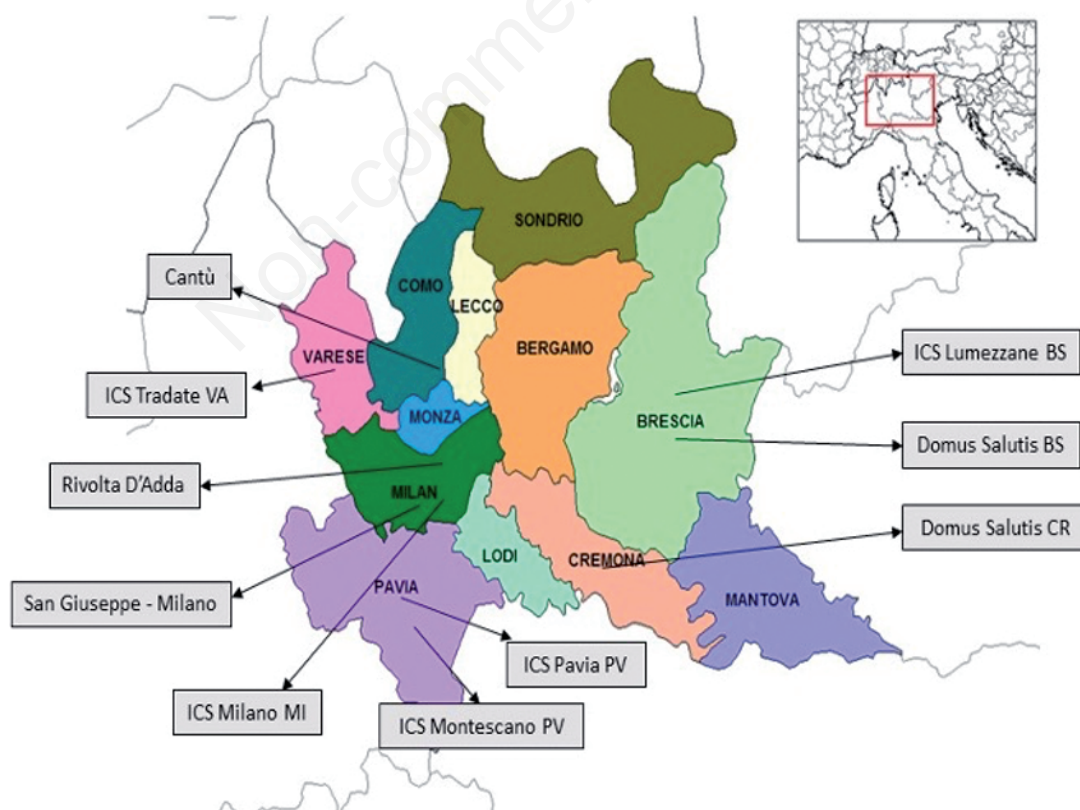


Figure 1. Distribution of Lombardy rehabilitative network.

Measurements

Data was recorded when patients were admitted to the rehabilitative hospital and on discharge. At admission the following data were collected: demographics, length of stay in acute hospital, use of oxygen supply, use of NIV or IMV and diagnosis of comorbidities by the Cumulative Illness Rating Scale (CIRS) [13].

Information about ADL independency and disability was recorded as follows: motor performance was assessed by the Barthel index (BI) [14], physical performance was assessed by the Short Physical Performance Battery (SPPB) [15,16], exercise tolerance was assessed by the 6 minutes walking test (6MWT) [17], dyspnoea during ADLs was assessed by the Barthel dyspnoea [18] and Medical Research Council (MRC) dyspnoea scale [19].

Data related to nutritional status (Malnutrition Universal Screening Tool - MUST) and risk of falls (Morse fall scale) were also collected at admission.

Pulmonary rehabilitation

In accordance with the Italian Position Paper, a multidisciplinary program was applied in all centres [20]. The best rehabilitation program for the patient was selected according to age, clinical severity, length of immobilization and comorbidities. Different modality of intervention, type, intensity and timing were considered. All patients began with a 20-min session per day and continued with a range of time between 30-60 min/session for once or twice per day. Sessions could be individual or in groups. Individual sessions involved pas-

sive mobilization, bed position changes, stand-up exercises, active exercises, free walking or walking with assistance, peripheral limb muscle strengthening and balance training. Group sessions involved strengthening, aerobic and balance exercises. Patients with a higher physical autonomy were also trained with cycle-ergometer or treadmill. Each patient started with a zero-training workload and progressively increased it until patient scored four or five points at dyspnoea or leg fatigue using the Borg scale [21]. During rehabilitation, patients were evaluated daily in order to tailor intervention type, intensity and/or length of the program.

Statistical analysis

Data were registered on a dedicated database (Excel®, Microsoft, Redmond, WA, USA). Continuous variables were expressed as mean and standard deviation (SD) and binary or categorical outcomes were described as percentage (%). Paired *t*-test was used for pre- to post-comparison; statistically significant value was set at $p < 0.05$.

Results

This study included 413 patients coming from the ten rehabilitation centres listed above. Demographics, physiological, and clinical characteristics of patients are shown in Table 1.

Most of the patients arrived in the rehabilitation units from acute hospital, while only 7.7% of patients arrived from home. Length of stay in an acute unit was less than 30 days for all

Table 1. Baseline demographics, clinical and functional data.

Patients, n	413
Sex, n (%)	286 (69.2%) M; 127 (30.8%) F
Age, years	70.97±11.76
BMI, kg/m ²	26.40±6.0
CIRS, score (279 pts)	3.03±1.90
Place of acute phase management, n (%)	hospital: 381 (92.3%); home: 32 (7.7%)
Length of stay in acute unit, day	24.77±19.04
Tracheostomy, n (%)	No=367 (88.9%); Yes=46 (11.1%)
CPAP/NIV, n (%)	No=286 (69.2%); Yes=127 (30.8%)
Length of stay in rehabilitative unit, day	25.73±17.46
FEV ₁ , % prd (50 pts)	75.88±17.89
FVC, % prd (50 pts)	73.66±19.83
IC, % prd (50 pts)	63.14±22.89
DLCO, % prd (26 pts)	50.35±22.45
PaO ₂ /FiO ₂ at admission (181 pts)	307.81±88.21
Barthel index, score (162 pts)	56.81±31.49
SPPB, score (143 pts)	4.61±4.04
Barthel dyspnoea, score (127 pts)	27.82±22.46
6MWT, meters (199 pts)	215.77±146.95
MRC, score (145 pts)	2.66±1.07
Place of discharge, n (%)	dead: 12 (2.9%); acute unit: 83 (20.1%); home: 318 (77.0%)

Data are expressed as mean±SD. In brackets number of patients with available data (n, number). BMI, body mass index; CIRS, cumulative illness rating score; CPAP, continuous positive airway pressure; NIV, non-invasive ventilation; FEV₁, forced expiratory volume 1; FVC, forced vital capacity; IC, inspiratory capacity; DLCO, carbon monoxide diffusing capacity (lung function); PaO₂, arterial pressure of oxygen; FiO₂, inspiratory fraction of oxygen; SPPB, short physical performance battery; MRC, MRC dyspnoea scale; 6MWT, six minutes walking test.

patients. All patients suffered from respiratory failure and many of them needed NIV; 11.14% of patients were admitted with tracheostomy and needing IMV. At least for the patients in which functional data were available, respiratory functional status seemed mildly compromised for lung function parameters and oxygenation, while severely impaired for diffusion capacity. At admission, at least for the patients in which disability data were available, patients presented high disability and a very low physical performance status assessed by Barthel index and SPPB, respectively. Barthel dyspnoea and MRC showed important dyspnoea during ADLs. Again, at least for the patients who performed the 6MWT, severe reduction in effort tolerance was found at the beginning of the rehabilitation program. On discharge the majority of patients were sent home and only a small group were transferred to an acute unit or passed away. Table 2 shows assessment/evaluation tests done by each centre according to habits, standards and organisational availability. BI and 6MWT were the most used, while MRC score was the less used outcome parameter.

Figure 2 shows percentage of patients admitted to the 5 main rehabilitative programs (passive/active limb mobilisation in bed;

transfer from bed to armchair; walking; balance; cycle-ergometer or treadmill). On discharge 91% of patients were able to walk with or without assistance. Patients performed a dedicated program to walking in 90.8%, transferring from bed to armchair in 77.5%, limb bed mobilisation (76%), balance in 71.2% and cycle-ergometer or treadmill training in 43.1%.

Table 3 shows a huge difference in admission, discharge and subsequent delta improvement in 6MWT, SPPB and Barthel index among different rehabilitative centres. In the whole sample, for motor Barthel index a delta improvement of 21.96 ± 24.74 score was obtained. The hospitals with the higher improvements were ICS Lumezzane and FTC Brescia. For SPPB, a delta of 3.37 score was obtained. The hospital with the highest performance was ICS of Tradate. For 6MWT a delta of 105.57 meters was calculated. FTC Brescia was the hospital with the best performance.

Table 4 shows differences in admission, discharge and subsequent delta improvement in MRC and Barthel dyspnoea among centres. For MRC score a delta of 0.96 was obtained. The ICS of Lumezzane was the hospital with the best result. For Barthel dyspnoea, a delta of 14.43 was reached; the hospital with the best

Table 2. Assessment/outcomes indices used by different network hospitals.

Rehabilitation Unit	Barthel index	MORSE	MUST	SPPB	MRC	Barthel dyspnoea	6MWT
ICS Milano	X	X	X			X	
ICS Lumezzane	X	X	X	X	X	X	X
ICS Montescano	X	X		X		X	
ICS Pavia	X	X	X	X		X	X
ICS Tradate	X	X	X	X			X
Sant'Antonio Abate, Cantù							X
FTC, Cremona	X					X	X
San Giuseppe, Milan	X				X		X
FTC, Brescia	X						X
Santa Marta, Cremona		X		X	X		X

MORSE, Morse fall scale; MUST, malnutrition universal screening tool; SPPB, short physical performance battery; MRC, MRC dyspnoea scale; 6MWT, six-minute walking test; FTC, Fondazione Teresa Camplani.

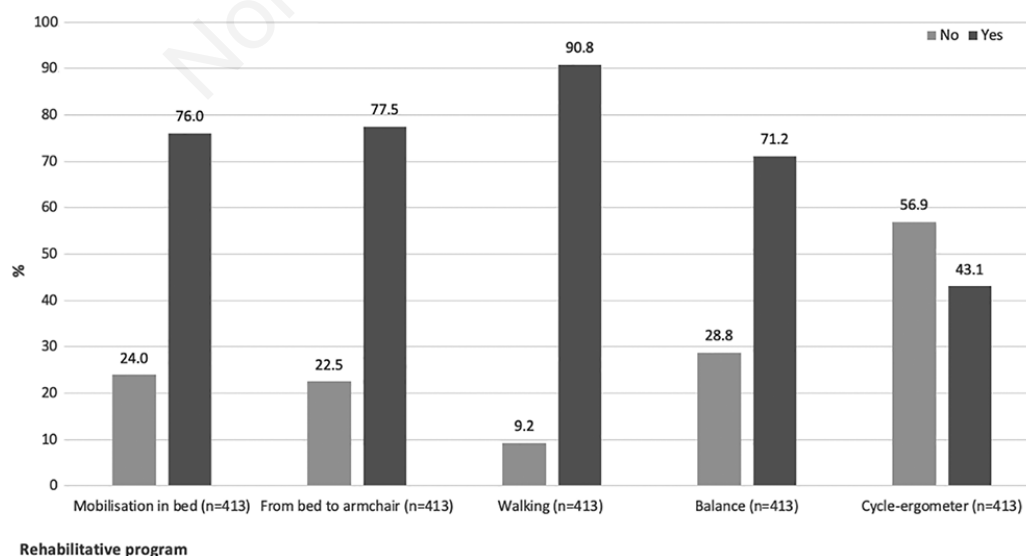


Figure 2. Percentage of patients admitted to the 5 main rehabilitative programs.

Table 3. Differences in “at admission and discharge” evaluations and changes of 6MWT, SPPB and Barthel index among centres.

Units	Barthel index (A)	Barthel index (D)	Δ	Units	SPPB (A)	SPPB (D)	Δ	Units	6MWT (A)	6MWT (D)	Δ
ICS Milano (9)	57.22±32.41	61.11±33.43	3.89±21.91	ICS Milano	5.53±4.93	8.75±3.12	3.22±2.94	ICS Milano	160.43±180.61	288.86±150.08	128.43±115.00
ICS Lumezzane (37)	65.54±32.76	90.81±14.22	25.27±29.84	ICS Lumezzane (32)	8.20±4.02	9.20±3.74	1.00±2.36	ICS Lumezzane (35)	254.61±116.10	377.94±113.68	123.33±81.01
ICS Montescano (2)	45.00±7.07	45.00±7.07	0.0±0.0	ICS Montescano (10)	5.00±4.12	8.45±3.79	3.45±3.39	ICS Montescano	228.25±247.08	318.63±272.76	90.38±131.42
ICS Pavia (18)	11.67±14.25	33.61±28.07	21.94±4.08	ICS Pavia (29)	5.75±4.62	10.00±2.27	4.25±3.96	ICS Tradate (8)	108.57±153.67	188.57±172.09	80.00±128.32
ICS Tradate (36)	59.03±23.66	78.89±24.90	19.86±15.92	ICS Tradate (8)	3.27±2.84	6.94±3.38	3.67±2.42	Cantù (7)	340.27±166.47	426.33±162.77	86.07±57.90
Cantù				Cantù	4.61±4.04	7.98±3.49*	3.37±2.89	FTC CR (15)	155.00±35.36	255.00±7.07	100.00±28.28
FTC CR (28)	67.71±26.13	91.54±20.06	23.82±22.05	FTC CR	21.96±24.74	21.96±24.74	0.0±0.0	San Giuseppe MI (2)	138.59±134.51	288.13±149.74	149.53±122.31
San Giuseppe MI (2)	71.50±12.02	88.50±16.26	17.00±4.24	San Giuseppe MI	56.81±31.49	78.77±29.66*	21.96±24.74	FTC BS (32)	243.87±86.45	343.20±104.74	99.33±82.80
FTC BS (30)	60.00±30.47	84.53±26.01	24.53±24.98	FTC BS				All (162)	213.14±146.78	326.29±145.08*	113.15±99.46
Santa Marta CR				Santa Marta CR (64)							
				All (143)							

In brackets the number of patients with available data for each hospital. A, admission; D, discharge; FTC, Fondazione Teresa Complani; CR, Cremona; BS, Brescia; MI, Milan. *refers to pre- to post-comparison p<0.001.

Table 4. Differences in “at admission and discharge” evaluations and changes of MRC and Barthel Dyspnoea among centres.

Rehabilitation Unit	MRC (A)	MRC (D)	Δ	Rehabilitation Unit	Barthel D (A)	Barthel D (D)	Δ
ICS Milano				ICS Milano			
ICS Lumezzane (29)	3.00±0.93	1.76±1.02	-1.24±0.79	ICS Lumezzane (24)	20.04±18.62	10.13±11.53	-9.92±11.48
ICS Montescano				ICS Montescano (19)	46.05±19.51	29.16±20.82	-16.89±25.93
ICS Pavia				ICS Pavia (26)	43.88±13.69	20.04±10.81	-23.85±13.81
ICS Tradate				ICS Tradate (35)	29.14±19.23	10.91±9.67	-18.23±17.34
Cantù				Cantù			
FTC CR				FTC CR (23)	0.70±1.14	0.00±0.00	-0.70±1.14
San Giuseppe MI (2)	3.50±0.71	2.50±0.71	-1.00±1.41	San Giuseppe MI			
FTC BS				FTC BS			
Santa Marta CR (114)	2.55±1.09	1.67±1.25	-0.89±0.88	Santa Marta CR			
All (145)	2.66±1.07	1.70±1.20*	-0.96±0.87	All (127)	27.82±22.46	13.39±14.75*	-14.43±17.35

In brackets the number of patients with available data for each hospital. A, admission; D, discharge; FTC, Fondazione Teresa Complani; CR, Cremona; BS, Brescia; MI, Milan. *refers to pre- to post-comparison p<0.001.

result was the Institute of Pavia. Oxygenation ($\text{PaO}_2/\text{FiO}_2$) improved in all 181 patients (from 307.81 ± 88.21 to 330.97 ± 76.83 ; $p < 0.001$).

Discussion

This study has shown, in a large sample of COVID-19 subjects that: i) patients with respiratory failure as a consequence of SARS-CoV-2 pneumonia and admitted in rehabilitative centres showed a reduced physical performance, key symptoms and severe disability at admission; ii) the most used measurement tools were 6MWT and Barthel Index, while the majority of proposed programs used walking assistance; iii) the majority of patients improved all rehabilitative outcomes.

Pulmonary rehabilitation is possible and effective in patients recovering from COVID-19: our findings may be useful to guide clinicians, politicians and health organisations to follow up and support management of patients surviving COVID-19.

Baseline assessment

It is necessary to have tools that objectively measure the functional consequences of COVID-19 disease in the short- and long-term. It has been reported that post-COVID-19 patients can have an impaired physical function when they are discharged, even after early mobilization [22]. Our results confirm these observations and extend to more severe patients directly transferred from acute care hospitals. By comparison [22], our patients suffered from more severe acute conditions shown by longer length of stay in acute care hospitals and by the high proportion of patients receiving mechanical ventilation as Invasive (including some tracheostomized) or NIV. The level and severity of comorbidities, as assessed by the CIRS index, was similar to those of patients reported. Thus, the need for validated outcome measures is of utmost importance. Standardisation of measures would allow to make better comparisons among studies and different follow-up time-points. The Barthel index and the six minutes walking test were the most used during patient stay in our network. The Barthel index was mainly used in the acute phase, whereas the 6MWT was used in interventional and follow-up studies. The 6MWT is the gold standard field exercise test and it has been validated for most chronic lung diseases. Eight centres out of ten used 6MWT to evaluate patients before and after rehabilitation. This test is sensitive, reproducible, easy to perform, and does not require any specialized equipment. In routine clinical practice, the Barthel Index is the most widely used scale to measure patients' motor and functional disabilities in activities of daily living (ADL). This index was developed for chronic and long-term hospital patients with neurological diseases to examine their performance before and after treatment. Five hospitals used SPPB test: this is a standardized objective tool which is rapid and simple to conduct and less influenced by cultural and educational background than other self-report measures. It has also been shown that SPPB is significantly related to the capacity to perform ADLs, such as changing and maintaining body position, carrying, moving, and handling objects, or walking and gait pattern. Several instruments are commonly used to measure different domains of dyspnoea such as sensory-perceptual experience, affective distress, symptom impact or burden. The most used scale to assess dyspnoea in daily life was

the modified Medical Research Council (mMRC) scale. Curci *et al.* found the most severe score (level 5) in 87.5 and 90.2% of COVID-19 patients [23]. Huang *et al.* [1] reported that, 6 months following disease onset, 26% of patients had mMRC levels greater than 1. Only one study [25] used the Barthel dyspnoea index, in a rehabilitative setting, and reported moderate levels of dyspnoea during activities of daily life.

Rehabilitative effects

Our pulmonary rehabilitation program was inspired by the Italian Position Paper dedicated to COVID-19 rehabilitation [5]. In real life, type, intensity, timing, and modality of intervention were tailored to the individual patients and according to local organization's protocol. The Sant'Antonio Abate Hospital (Cantù), the San Giuseppe Hospital (Milan), the FTC (Cremona and Brescia) and the ICS Maugeri in Lumezzane admitted the most complicated patients with a very low level of effort tolerance. An improvement in 6MWT of 105.57 meters in the whole group confirmed that the majority of patients reached the minimum clinically significant difference of 54 meters proposed for COPD patients. According to Perera *et al.* [26] one point is considered as the minimum clinically important difference (MCID) for SPPB and all studied patients who underwent this test got better after the rehabilitation program. Another tool is the MRC questionnaire, used mainly in COPD patients to measure perceived respiratory disease in activity of daily living. The MRC questionnaire was also only used at ICS Maugeri Lumezzane and San Giuseppe Milan resulting in an improvement over the rehabilitation program. Barthel dyspnoea is another questionnaire to assess patient's respiratory disease in activity of daily living. Four centres used it with very different scores at admission. ICS Maugeri Montescano and ICS Maugeri Pavia had the highest score showing a very high level of dyspnoea, while patients at FTC Cremona presented low level of dyspnoea. As a consequence, the first two centres had a better improvement over rehabilitation program. A wide range of different impairment in physical performance and in amount of response to rehabilitation programs was reported with the use of these tools. Differences among centres may be explained by different volumes of patients admitted, different admission severity levels and different assessment tools compared with different organisations offering rehabilitative programs.

Practical implications

The presented data shows the strong response, efficiency and effectiveness of the Lombard respiratory rehabilitation network, although still marked by a strong organizational heterogeneity and entry criteria. These pathways are often underutilized due to poor economic recognition though the enormous consumption of resources that specialist rehabilitation requires for severely chronically unstable and disabled patients [27]. In the era of the COVID-19 pandemic, the Lombard rehabilitation network offered strong support for severely affected COVID-19 patients to improve disability, quality of life and symptoms. The findings show the need to increase and develop the model of clinical care networks and emphasize the integration between hospital and territorial services in order to combine continuity of care and sustainability of the system.

Limitations of the study

This design allowed including a large number of patients but, due to the retrospective nature of the study, a lot of data was missing and this is an important limitation. The results of an uncontrolled study may be difficult to interpret: a positive effect in the long-term follow-up of these patients without a rehabilitative intervention may not be excluded. An untreated group would be unethical given the undisputed benefits of pulmonary rehabilitation or simple physical activity.

Conclusions

This study has shown, in a large sample of COVID-19 subjects that, patients admitted in rehabilitative centres present a reduced physical performance, key symptoms and severe disability. 6MWT and Barthel index as measurement tools and walking as a program are the most used during the rehabilitative phase. The majority of patients improved in all outcomes with high variability among participating centres. Better standardisation is mandatory for future studies with higher methodological quality with the choice, timing and interpretation of measures of physical performance and rehabilitative prescription.

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