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Review Article

Functional Evolution after an Adapted Physical Activity during Long COVID

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Abstract

Background: The COVID-19 pandemic was responsible for chronic forms including long COVID which resulted in a loss of autonomy and function. The objective of this work was to evaluate the short and medium-term impact on the autonomy and function of an Adapted Physical Activity (APA) in patients suffering from long COVID.

Methods: Prospective, longitudinal, observational study that included patients with long COVID recruited over 21 months. The patients benefited from a rehabilitation program twice a week for 6 weeks. The following were assessed: pain (VAS), dyspnea (Borg Scale), fatigue (Pichot Scale), activity limitations (FIM), degree of breathlessness in activities of daily living (mMRC), balance and walking (STST, TMWT) before integration into the protocol (E1), immediately at the end of the 12 sessions (E2) and after 6 months (E3).

Results: Fifty patients were included with a mean age of 52 years. The main symptoms were asthenia and exertional dyspnea. We noted a significant improvement of pain after the APA protocol at E2 and E3.Twenty-six patients still had dyspnea after rehabilitation ($p<0.001$) and 21 at E3($p<0.001$). At E2 there were as many patients with a Borg above the median as below the median and at E3 the majority of patients had a Borg below the median. Ten patients had decreased fatigue at E2 ($p<0.001$) and 12 patients at E3. Forty-four patients improved their FIM ($p<0.0001$) at E2 and 36 at E3. Twenty-six patients were still dyspneic after rehabilitation ($p<0.001$) and 21 at E3 ($p<0.001$). The walk speed and endurance increased at E2 and E3.

Conclusion: Our study highlights the strongly positive impact of exercise on autonomy and functional sequelae in long COVID.

Keywords: Long COVID; Adapted physical activity; Rehabilitation; Dyspnea; Fatigue; Activity limitation; Balance; Walking

Introduction

SARS-COV2 infection can be responsible for major forms involving the vital prognosis but also for less severe forms compromising the functional prognosis [1]. Whatever the initial clinical form observed, residual symptoms may be found which extend beyond 4 weeks of the COVID attack [2]. There are many symptoms that can affect several systems at the same time. These may include fatigue, dyspnea, cough, chest pain, disturbances in concentration and memory, headache, disturbances of smell and taste, myalgia, diarrhea or loss of appetite, not attributable to other diagnoses [3]. This symptomatology is grouped in a no so logical frame work called COVID long. This state can determine a limitation of activity as well as a restriction of participation in the affected person with consequently a major societal impact requiring the establishment of appropriate public policies. Adapted Physical Activity (APA) is part of the proposed therapeutic arsenal. The majority of scientific work has highlight edits short-term positive impact in patients suffering from long COVID [4], while its medium-term impact remains largely unexplored, whence the interest we have shown to this subject.

The objective of our work was to evaluate the short and medium term impact of an APA protocol on the autonomy and function of patients suffering from long COVID.

Materials and Methods

Study design

We conducted a monocentric, observational, prospective and longitudinal study on a single group of patients in three steps. Our study focused on patients with long COVID, recruited from the Physical Medicine and Rehabilitation (PMR) B department at the Mohamed Kassab Institute of Orthopedics (IMOK) over a 21-month period (June 2020-March 2022).

Patients were referred from several medical departments for Post-COVID cardiopulmonary rehabilitation. They were aged between 18 and 85. They were suffering from a symptomatology that matched with the definition of long COVID, had no contraindications to physical exercise and had given their oral consent to participate in our protocol. We did not include children, patients over 85 years of age, oxygen-dependent patients, patients with an evolving COVID (long COVID symptoms <4 weeks), patients with a cognitive or psychiatric disorder that could affect the reliability of the assessment, pregnancies and patients who refused to participate in the study.

We excluded patients who did not complete the APA protocol, those reinfected with SARS-COV2 between the initial (E1) and final (E3) assessment, patients who were unable to attend the intermediate (E2) and/or E3 assessment, and those who developed in tolerance or malaise during the APA sessions. A personalised APA protocol (Figure

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1) was set up on an outpatient basis over a 6-week period, with 2 face-to-face 30-minute sessions per week. The APA protocol differed from one patient to another depending on the level of cardio respiratory rehabilitation. Each programme included respiratory training, a bronchial decongestion programme and physical rehabilitation with regular adaptation of exercise intensity during the entire session. Each patient was evaluated three times (Figure 2):

- -E1: Initial evaluation before integration into the rehabilitation protocol.
- -E2: Intermediate evaluation at the end of the rehabilitation protocol (short-term evaluation).
- -E3: Final evaluation 6 months after the end of the rehabilitation protocol (medium-term evaluation).

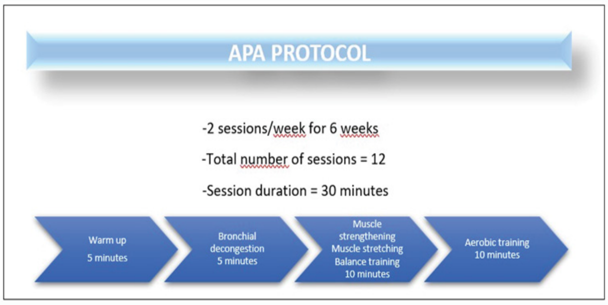

Figure 1: The APA protocol process.

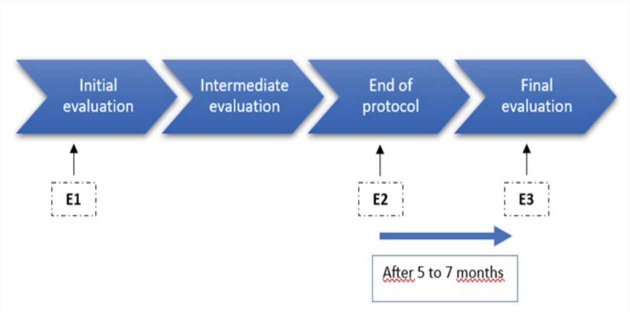

Figure 2: Study evaluation process.

We collected our patient's socio-demographic data, their comorbidities, the form of COVID-19 involvement, the most common symptoms in the initial and residual phases, and the need for hospitalisation or oxygen therapy in the acute phase. We also recorded the anthropometric parameters (weight, height and BMI) for all our patients.

We assessed impairments before and after the APA protocol. The main impairments assessed were pain using the Visual Analogue Scale (VAS) from 0 (no pain) to 10 (maximum level of pain), dyspnea using the Borg Scale from 0 (no dyspnea) to 10 (very, very severe dyspnea) and fatigue using the Pichot scale (a score above 22 was in favor of extreme fatigue). Activity limitations were also assessed globally using the generic scale for Functional Independence Measurement (FIM). This scale consists of 18 items assessing 6 functional domains divided into 2 categories: motor (13 items) and cognitive (5 items). Each FIM item is graded on a 7-point Likert scale, and the result indicates the level of assistance required to complete each item (1=total assistance, 7= total independence).

The overall score is between 18 and 126, where 18 represents complete dependence and 126 represents complete independence. The cut-off point of 80 represents the need to be helped by a third part.

We also specifically assessed the degree of breathlessness in activities of daily living using the modified Medical Research Council (mMRC) dyspnea scale (Appendix 1), rated between 0 (no dyspnea except with sustained effort) and 4 (dyspnea prevents leaving the house/present when dressing or undressing).

We also assessed activity limitations in terms of balance and walking, using the Sit to Stand Test (STST) and the 10-metre walk test (TMWT) respectively.

Statistical analysis

The results were coded using SPSS 26.0 "The Statistical Package of Social Science". First, the normality test was performed to check whether the distribution of the population based on the variables studied obeyed a normal distribution. This was followed by a descriptive analysis. For qualitative variables, simple frequencies and relative frequencies were calculated. For quantitative variables, the medians, quartiles P25 and P75, mode and extreme minimum (min) and maximum (max) values were calculated. Averages and extreme values were preferred to describe the distribution of universal variables such as age. In some cases, means and Standard Deviations (SD) have also been calculated. Then, bivariate analysis was carried out to identify associations. Because of the non-normality of the distribution of the variables studied non-parametric tests were used. The Mann-Whitney U test was used to compare medians between two groups. The Kruskal-Wallis H test was used to compare medians between several groups.

Spear man correlations were used to study bilateral associations between quantitative variables, specifying p as well as Spearman's rho, which reflects the strength and direction of the association.

The r varies from -1 to 1: -1: the correlation is negative: the more a variable increases, the more the variable studied decreases. 0: no correlation: the variation of one variable does not modify the variation of the variable studied. 1: the correlation is positive: the more a variable increases, the more the variable studied increases. The stronger the association is, the closer is the r to 1 or -1. Simple linear regression was used to detect linearity (R^2). Non-Significant (NS) associations were not subjected to linear regression. The R^2 varies from 0 to 1. The closer the R^2 is to 1, the better the linearity. For the r in absolute value and the R^2, the interpretation of the results was as indicated below:

- [0-0.299]: The association or linearity is low.
- [0.300-0.499]: The association or linearity is moderate.
- [0.500-1]: The association or linearity is high.

The confidence interval was predicted at 95% and the significance cut-off point was set at 0.05. Values with a $p<0.05$ were therefore considered significant.

Results

Patient selection procedure

Our population included 50 patients with long-COVID who matched our requirement (Figure 3).

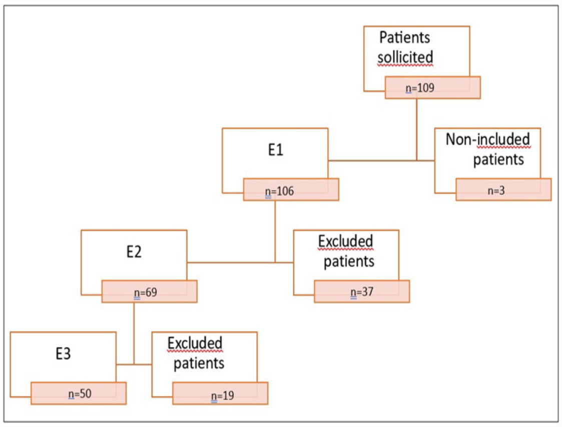

Figure 3: Flow chart of study participation.

Characteristics of the population

As shown in Table 1, the mean age of our population was 52 years, with a gender ratio of 1.27. The most common comorbidities were diabetes (24%) and hypertension (22%). The predominant form of initial COVID-19 disease was mild (48%), with asthenia (66%) and effort dyspnea (66%) as the main symptoms in the initial and residual stages. More than half of our patients required hospitalisation and 56% required oxygen therapy. Clinical assessment showed that the majority of our patients were overweight (52%). In addition, 43 patients were initially suffering from dyspnea as assessed by the mMRC scale.

Evolution of Disabilities in Relation with Long COVID

Pain

Eighteen patients complained of nociceptive pain at rest and during exercise, mainly in the rachis (n=10), lower limbs (n=6) and upper limbs (n=2). These pains disappeared in 8 patients at E2 and in 2 other patients at E3.

However, two patients complained of neuropathic pain, which disappeared in one patient at E2 and did not reappear at E3.

Dyspnea

Forty-three patients were initially dyspneic as assessed by the mMRC scale (Figure 4). Twenty-six patients still had dyspnea after rehabilitation ($p<0.001$) and 21 others were still dyspneic at E3 ($p<0.001$).

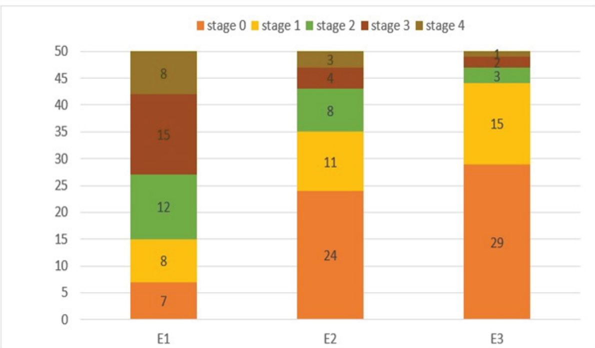

Figure 4: Distribution of patients according to stage on the mMRC scale for the three.

Table 1: Population characteristics.

	n=50
Demographic data	
Age (years-old)	52
Female gender	22 (44%)
BMI (Kg/m^2)	30,74 ± 4,35
Education (n, %)	
Primary	7 (14%)
Secondary	12 (24%)
University	26 (52%)
Tobacco (n, %)	
Smoking	9 (18%)
Non-smoking	41 (82%)
Covid data	
Severity (n, %)	
Mild	24 (48%)
Moderate	12 (24%)
Severe	14 (28%)
Care environment (n,%)	
Homecare	26 (52%)
Hospital care	24 (48%)
Medical Department	14 (28%)
Intensive care unit	10 (20%)
Length of hospital stay (days)	20 [2-65]
Signs et symptoms of long covid (disabilities) (n, %)	
Respiratory symptoms	
Effort dyspnea	33 (66%)
Rest dyspnea	12 (24%)
Dry cough	15 (30%)
Multiple pain	
Chest pain	10 (20%)
Headache	2 (4%)
Myalgia	13 (26%)
Gastrointestinal disorders	
Dysphagia	2 (4%)
Sensory anomaly	
Agueusia	4 (8%)
Anosmia	4 (8%)
Neurological disorders	
Stroke	1 (2%)
Memory disorders	10 (20%)
Comorbidities	
Diabete	12 (24%)
Hypertension	11 (22%)
Dyslipidemia	5 (10%)
Coronary artery disease	3 (6%)
Asthma	2 (4%)
Epilepsy	2 (4%)
Chronic bronchitis	1 (2%)
Stroke	1 (2%)

Taking into account the 3 assessments (E1, E2 and E3), the median of the Borg scale was 3.5 with a min of 0 and a max of 10. At the first assessment E1 (Figure 5), the majority of patients with long COVID (41 patients) had a Borg above the median. Then, at E2 there were approximately as many patients with a Borg above the median as there were patients with a Borg below the median. Finally, at the third assessment, the majority of patients had a Borg below the median (39 patients). The difference between the medians of the Borg scale at the three assessments was significant, with $p<0.0001$.

Fatigue

Initially, the median of the Pichot scale was 19 with a minimum value of 0 and a maximum value of 32 (Figure 6). Ten patients (20%) had decreased fatigue at E2 ($p<0.001$) with the median decreasing to 14.5 (min=0; max=35). By E3, 12 (24%) patients had experienced a decrease in fatigue with the median falling to 12 (min=0; max=29).

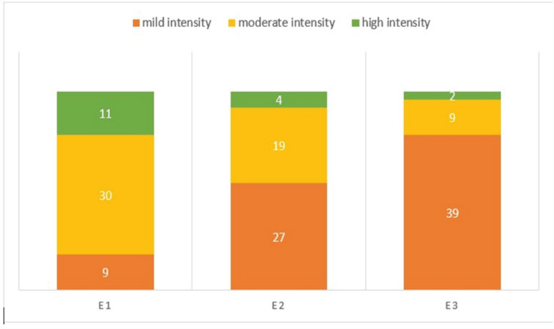

Figure 5: Distribution of the perception of the intensity of effort based on the Borg scale during the three valuations.

Evolution of Disabilities Linked to Long COVID

Evolution of autonomy

Two patients had an initial FIM below 80 and were totally dependent on a third part. The median FIM was 110 Table 2. At E2, 44 patients improved their FIM (p<0.0001) and the median value increased to 120 with only one patient maintaining a value below 80. At E3, 36 other patients improved heir FIM again (p<0.0001) with a median value of 122 and only one below 80. The most affected item in the three assessments was climbing stairs.

Progression of activity limitation related to dyspnea

Twenty-six patients were still dyspneic after rehabilitation (p<0.001) and 21 others were still dyspneic at E3 (p<0.001) (Figure 4).

In addition, a statistically significant association was found between the global FIM and the mMRC score during the three assessments, with a negative correlation Table 3.

Changes in activity limitations related to balance and walking

In patients with long COVID, the mean walk speed was 0.92 m/s (min=0.2 m/s; max=2.16 m/s). This speed increased at E2 (p<0.0001) in 41 patients with an average of 1.12 m/s (min=0.33 m/s; max=1.89 m/s) and continued to increase at E3 (p<0.0001) in 25 patients with an average of 1.1 m/s (min=0.38 m/s; max of 1.8 m/s). It should be noted that only one patient required technical assistance to walk during the 3 assessments.

In addition, the average of our patients' STST was 8 repetitions (min=0 reps; max=13 reps) after COVID-19. An improvement in endurance was observed in 46 patients at E2 and continued to improve in 23 patients at E3.

Discussion

Review of the main results

The mean age of our population was 52 years, with a gender ratio of 1.27. The most common comorbidities were diabetes (24%) and hypertension (22%). The predominant form of initial COVID-19 infection was mild (48%), with asthenia (66%) and effort dyspnea (66%) as the main symptoms in the initial and residual phases. More than half of our patients required hospitalisation and 56% required oxygen therapy. Clinical assessment showed that the majority of our patients were obese (52%). We also noticed: Short-term improvement (E2) with an increase in the medium-term gain (E3) in dyspnea

Table 2: The central and dispersion values of the FIM in the three valuations.

	E1	E2	E3
Mediane	110	120	122
Percentile 25	101	115	119,75
75	117,5	122	124
Minimum	63	70	78
Maximum	126	126	126

Table 3: Study of the association between FIM and mMRC in the three assessments.

	p(r)E1	p(r)E2	p(r)E3
FIM / mMRC	0,009 (-0,367)	<0,0001 (-0,491)	<0,0001 (-0,549)

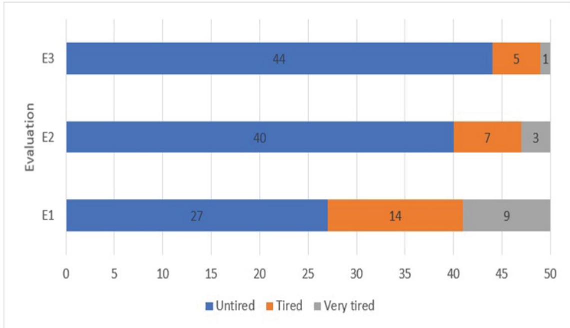

Figure 6: Distribution of fatigue according to the Pichot scale during the three assessments.

on the Borg and mMRC scales. Indeed, 24 patients were no longer dyspneic at E2 and 28 at E3. We also noted a decrease in nociceptive pain in the short and medium term. In terms of fatigue, we obtained an improvement in the Pichot scale at E2 (<0.001) and E3 (<0.001). From a functional point of view, all the parameters of our assessment improved significantly. We observed an increase in FIM in 44 patients at E2 and in 36 patients at E3 (p<0.001). We also noted an increase in walking speed (p<0.001) and in the number of STST repetitions (p<0.001). Forty-six patients had increased in their number of STST repetitions at E2 and 23 at E3. Short-term improvement (E2) with preservation of the gain in the medium term (E3) was observed for neuropathic pain. We noticed a regression at E2 which was maintained at E3.

Strengths and limitations

The main strength of our study is its originality. To our knowledge, it is the first study to evaluate not only the short-term impact of an exercise-based rehabilitation protocol in patients suffering from long COVID, but also the medium-term impact. In fact, the literature has mostly focused on the immediate impact of exercise rehabilitation, without any real follow-up of the evolution of the gain over time. In addition, we ensured that we used scores validated in the Arabic language, which reduces assessment bias and increases the scientific value of our work.

In addition, several limitations must be taken into account when interpreting the results of our study. Firstly, there was no reference control group. A randomized controlled trial would have given more value to our work. Indeed, no causal relationship with APA can be established with confidence because of our observational study design. However, conducting a randomized controlled trial on the effect of adapted physical activity may be considered unethical. Indeed, a control group cannot be deprived of a potential treatment because of an ongoing study. Consequently, the improvement observed in our study could also be due to the normal recovery process after COVID-19 disease.

The second weakness of our study was the small size of the population studied, which is explained by the difficulties of recruitment that we faced. In fact, our study began during the COVID-19 pandemic, which made moving around difficult, on the one hand because of the health restrictions faced by the country, and on the other because of the refusal of patients who had to go to hospital twice a week for 6 weeks to follow the APA protocol that we had established. We also had to deal with a large number of patients who were lost to follow-up. In fact, several patients did not complete the three assessments, which could have been completed by telephone for some scales and scores, but our clinical assessment would have been missing several parameters. In addition, patients had to be referred from other departments with different specialties, because the physical medicine and functional rehabilitation departments are third-line services. Finally, we received several patients whose respiratory or cardiac status was fragile or who were on home oxygen therapy, which mean that they could not be included in our study.

Discussion of the main results

Concerning socio-demographic data, [5] found a mean age of 49 years in their study conducted in Colombia. In Italy, a meta-analysis of 15 studies on 47910 patients with long COVID [6] found an average age of 46.8 ± 10.7 years. The results of our study were similar to those found in the literature. The mean age of our population was 52 years, with a predominant age distribution between 50 and 60 years. This could be explained by the fact that the under-50s in our population are negligent when it comes to their health. Indeed, access to care for patients who did not have a permanent job or health care was quite difficult. Not to mention the fact that our patients had to take time off work twice a week for 6 weeks to follow our rehabilitation protocol. It would have been more interesting to carry out the adapted physical activity sessions in the afternoons, so that the "younger" age group could have benefited more easily. In terms of gender ratio, [7,8] found that the majority of women were affected by persistent COVID symptoms. Indeed, the female sex has even been designated as a risk factor for long COVID [9].

These results found in the literature were not consistent with our study. In fact, our population was predominantly made up of men, with a gender ratio of 1.27. Our results could be explained by a neglect of medical care on the part of women, as the many tasks they perform are not compatible with a 6-week rehabilitation period. This was also confirmed by the study by [4], in which rehabilitation required 6 weeks of visits to an ambulatory pulmonary rehabilitation centre, and only 43% of patients were female.

Furthermore, concerning the most frequent co-morbidities in terms of long COVID, a meta-analysis [3] based on 45 articles indexed on Pubmed showed that arterial hypertension and diabetes were present in 35% and 26% of patients with persistent Post-COVID symptoms. Moreover, [9] demonstrated a bidirectional relationship between COVID-19 and diabetes. In fact, this viral attack is associated with a disturbance in glycemic levels, a revelation of pre-existing diabetes and the long-term diabetes is associated with the chronicity of COVID-19 symptoms in survivors.

A Tunisian study conducted at the Abderrahmen Mami Hospital also showed that diabetes and hypertension were the most frequent co-morbidities associated with long COVID [10], as did another study conducted in Sfax [11]. These results from the literature are in line with our own. Indeed, more than a third of our patients had diabetes and hypertension.

Concerning functional signs, [3] described that fatigue was the most common symptom of Post-COVID syndrome with an incidence up to 72% and that dyspnea was the second most common symptom with an incidence up to 65.6%. In our study, we found the same results. Indeed, the main complaints reported in our study were fatigue and dyspnea in 66% of patients. This fatigue has become a real public health problem. In fact, one study showed that more than 50% of patients with SARS-COV-2 suffered from chronic fatigue 10 weeks after their infection [9]. Its mechanisms are thought to be similar to those of other viral infections. It is thought to be the result of chronic oxidative and nitrosative stress, low-grade inflammation and altered production of thermo shock proteins. The dyspnea observed during long COVID could also be multi factorial [12]. Weakness of the inspiratory muscles [13] is thought to be the main cause. What's more, invasive mechanical ventilation lasting more than 7 days would lead to atrophy of the inspiratory muscles with reduced inspiratory muscle strength, which would be responsible for this hyperventilation.

This was supported by the improvement of the dyspnea after targeted high-intensity training of the inspiratory muscles [13], which has been shown to be effective in chronic lung disease [14] and also in heart failure [15]. In addition, this weakness of the inspiratory muscles is often associated with pulmonary fibrosis induced by cytokine storms in the acute phase [16], bronchiectasis and pulmonary vascular disease, resulting in chronic dyspnea [17].

In terms of weight, in a study by [18] performed in the United Kingdom on 29869 patients with long COVID patients, 28.8% were overweight and 30.9% were obese. Indeed, patients with a BMI over 30 kg/m^2 had a 10% relative increase in the risk of developing symptoms of long COVID compared with those with a BMI of 18.5 kg/m^2 to 25 kg/m^2. This has also been demonstrated in other studies [3]. A baseline BMI in the overweight or obese category was associated with an increased risk of symptoms persisting beyond 4 weeks [19]. These results were in line with our own, with 44% of patients being overweight and 52% obese. Therefore, overweight and obese people should be subject to targeted active surveillance and a BMI greater than 25 kg/m^2 should require a particular level of attention in hospital [16].

In terms of function, [20] found in their observational cross-sectional study that a large proportion of patients hospitalised for COVID-19 had a deterioration in their functional status 6 months after hospitalisation [21]. Carried out an observational longitudinal study in two outpatient centres specialised in respiratory rehabilitation in France. The study was conducted for a period of one year (April 2020-April 2021). It included 39 patients' suffering from prolonged functional sequels. Respiratory rehabilitation was conducted in the form of 1 hour and a half sessions three times a week, and included strength training and aerobic exercise. An initial assessment was carried out at the time of referral for rehabilitation and a second assessment after two months of rehabilitation. A statistically significant improvement in walking speed was found, as well as an increase in the number of STST repetitions, reflecting a better exercise capacity. These same results were found by [4,22]. Furthermore, [23] carried out a study in Switzerland between March and December 2020, including 99 patients divided into two groups (a group of patients with long

COVID and a group of patients with pulmonary diseases). They benefited from 3 weeks of APA at a frequency of 5 to 6 sessions per week. It was a multimodal programme customized to the severity of the disease, including endurance and muscle-strengthening exercises. There was a significant improvement in measures of FIM and walking speed. This multivariate analysis clearly demonstrated that COVID-19 itself had a strong impact on changes in FIM and walking speed [24]. These results from the literature were in line with our own. Indeed, in our study, we found an improvement in global MIF in more than half of patients after our APA protocol. This increase was even greater 6 months later. We also found an improvement in walking speed at E2, which was maintained at E3, and an improvement in STST at E2, which continued to improve at E3. This short-term improvement in functional assessment parameters can be explained by the greater potential for recovery in patients with long COVID compared with patients with chronic illnesses. However, the improvement in the medium term can be explained by the consolidation of the progress obtained during our APA sessions by carrying out the same maintenance exercises at home.

Conclusion

At the end of this study, and in the light of the results found indicating the benefits of APA in the treatment of long COVID, it should be recommended to systematically integrate this intervention into the management of all these patients. It would be ideal to establish guidelines for the treatment of patients with long COVID in Tunisia. But also, considering that the risk factors for the transition to chronicity after an acute COVID infection have been identified in the literature, an upstream intervention should be proposed, and the population could be made much more aware of the need for physical activity in all patients suffering from acute COVID, as well as a balanced diet, weight reduction and balancing of diseases.

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