Original Paper

Positive Effects of Pulmonary Rehabilitation Among Patients with Obstructive Ventilatory Dysfunction Post COVID-19

GABRIELA-MARINA BRÎNDUȘ[1], EUGENIA-ANDREEA MARCU[1], MIHAI OLTEANU[2], MAGDALENA RODICA TRĂISTARU[3]

[1]PhD Student, Doctoral School, University of Medicine and Pharmacy of Craiova, Romania

[2]Internal Medicine-Department of Pulmonology, University of Medicine and Pharmacy of Craiova, Romania

[3]Department of Physical and Rehabilitation Medicine, University of Medicine and Pharmacy of Craiova, Romania

ABSTRACT: Background.SARS-CoV-2 (Severe Acute Respiratory Syndrome Coronavirus-2) infection appeared for the first time in Wuhan, China in December 2019, and in March 2020 it was declared a pandemic by the World Health Organization (WHO). Thus, a new disease was registered-COVID-19 (Coronavirus Disease 2019). Our study followed the patients who had the diagnosis of obstructive ventilatory dysfunction in their personal pathological antecedents, who tested positive for SARS-CoV-2 infection. The patients were in the hospital records with chronic obstructive pulmonary disease (COPD) or asthma. After discharge, patients had a number of outstanding symptoms: fatigue, cough, dyspnea, mental and cognitive disorders, palpitations, headaches, dysfunctions of taste and smell. All patients underwent pulmonary rehabilitation after hospitalization. Aims. In this study, we looked at the benefits of respiratory rehabilitation over a period of six months after SARS-CoV-2 infection. The medical rehabilitation program included physical training, muscle training, nutritional support, psychological support and patient education. Methods. A retrospective study was defined between April 2021-December 2021, including 72 patients who had SARS-CoV-2 infection and who presented various symptoms on discharge. The study was carried out at the Clinical Hospital of Infectious Disease and Pneumoftiziology "Victor Babeș" from Craiova-Pulmonology Department. These patients had a history of obstructive ventilatory dysfunction: asthma or COPD. Patients were monitored during the respiratory rehabilitation program at 3 and 6 months after discharge. Results. An improvement in clinical and functional parameters was obtained as a result of the pulmonary rehabilitation. Conclusions. Patients with COPD are increase risk to develop severe forms of COVID-19. Smoking is an important risk factor for SARS-CoV-2 infection and obstructive ventilatory dysfunction. Vaccination against SARS-CoV-2 infection is effective, being associated with mild forms of COVID-19. Pulmonary rehabilitation is a key point in the management of patients with COVID-19, improving exercise capacity, reducing dyspnea, improving health, increasing oxygen saturation and quality of life.

KEYWORDS: *Pulmonary rehabilitation, COPD, asthma, post COVID-19.*

Introduction

SARS-CoV-2 (Severe Acute Respiratory Syndrome Coronavirus-2) infection appeared for the first time in Wuhan, China in December 2019, and in March 2020 it was declared a pandemic by the World Health Organization (WHO) [1].

Thus, a new disease was registered-COVID-19 (Coronavirus Disease 2019).

Our study followed the patients who had the diagnosis of obstructive ventilatory dysfunction in their personal pathological antecedents, who tested positive for SARS-CoV-2 infection.

The patients were in the hospital records with chronic obstructive pulmonary disease (COPD) or asthma.

After discharge, patients had a number of outstanding symptoms: fatigue, cough, dyspnea, mental and cognitive disorders, palpitations, headaches, dysfunctions of taste and smell.

All patients underwent pulmonary rehabilitation after hospitalization.

The latest research demonstrates that asthma remains the most common chronic inflammatory lung disease in the world, and SARS-CoV-2 causes a marked inflammation in the upper and lower respiratory tracts, with hypotheses being issued regarding the clinical and pathophysiological association between them [2].

Patients with COPD present a high risk of decompensation when infected with SARS-CoV-2.

The studies carried out so far show an increased expression of the angiotensin-converting enzyme 2 (ACE2) of the SARS-CoV-2 receptor, but the pathophysiological mechanism is unrevealed [3].

Pulmonary rehabilitation is defined as an important department of medicine, being individualized according to the needs of each patient, trying to identify all symptoms in order to treat them [4].

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It is known that pulmonary rehabilitation is effective in the treatment of patients with COPD, having effects such as improving symptoms and increasing the quality of life.

Due to the fact that COPD patients are old and have comorbidities, especially diabetes, heart failure, hypertension, coagulation disorders, they are more prone to severe forms of COVID-19 [5].

It is also known that pulmonary rehabilitation is an integrated part of the treatment of patients with asthma, in all stages mentioned by GINA (Global Initiative for Asthma), because it determines the control of nocturnal and daytime symptoms, decreasing the need for medication and reducing number of exacerbations [6].

During the pandemic, it was assumed that there is a relationship between patients with chronic respiratory diseases and COVID-19, so that this association causes the appearance of complications, the increase of hospitalization days and the faster deterioration of the patients' physical condition.

Moreover, chronic respiratory diseases can enlarge morbidity and mortality during the pandemic caused by SARS-CoV-2 infection.

So that, the need to institute pulmonary rehabilitation as early as possible is a key point in treating and preventing complications in patients with history of lung diseases and COVID-19 [7].

Recent evidence shows that the early initiation of pulmonary rehabilitation dramatically influenced the prognosis of patients, increased exercise tolerance, reduced the occurrence of complications and increased the quality of life, assessed through the satisfaction questionnaire [8].

In order for patients to be able to resume their daily activities, reduce the degree of anxiety, increase their physical capacity and avoid the onset of depression, especially patients from rural areas, with several associated diseases, the pulmonary rehabilitation program must have a complex management [9].

Therefore, the respiratory rehabilitation program should be individualized according to the needs of each patient, because they present different stages of the disease, with distinct degrees of severity.

It is also very important to take into account the preferences of the patients [10].

In the case of patients diagnosed with COVID-19, a multidisciplinary approach is necessary to start the respiratory rehabilitation program.

Exercises are performed to remove bronchial secretions, prevent bedsores, restore mobility, effect physiological swallowing [11].

Objectives

The objectives of this study are to find out the effects of pulmonary rehabilitation after discharge of patients with COVID-19 and obstructive ventilatory dysfunction.

It should be noted that patients with moderate or severe forms of COVID-19 have also developed restrictive ventilatory dysfunction due to fibrosis lesions.

Hypothesis

In this study, we looked at the benefits of respiratory rehabilitation over a period of six months after SARS-CoV-2 infection.

The kinetic exercises in the respiratory rehabilitation program were performed depending on the degree of severity of the disease and the tolerance of the patients.

The medical rehabilitation program included physical training, muscle training, nutritional support, psychological support and patient education.

Material and Methods

The study followed the principle of the Declaration of Helsinki and was accepted by the Ethics Committee of the hospital no. 137/07.12.2020.

All participants who agreed to be part of the study signed an informed consent upon admission for the processing of personal data.

Our research involved 72 sufferers who were hospitalized for COVID-19 and who had various symptoms on discharge.

These patients had a history of obstructive ventilatory dysfunction.

Research protocol

Period and place of the research

We performed a retrospective study, between April 2021-December 2021, in the Pulmonology Department of the Clinical Hospital of Infectious Diseases and Pneumoftziology "Victor Babeș", Craiova.

Patients were monitored during the respiratory rehabilitation program at 3 and 6 months after discharge.

Patients performed recovery exercises at home with a physiotherapist, in department of Psysical Medicine and Rehabilitation or through telemedicine, depending on the possibilities.

Subjects and groups

The 72 hospitalized patients who presented with various forms of COVID-19 were split up into 2 lots: the first lot S1-consists of 35 patients diagnosed with asthma, and the second lot S2-includes 37 patients diagnosed with COPD.

The patients included in the study had to comply with the following inclusion criteria: asthma and COPD diagnoses were correctly established according to specific guidelines; all patients were testedby Real-Time Reverse Transcription-Polymerase Chain Reaction (RT-PCR) and got positive for SARS-CoV-2 infection, rapid antigen tests results were excluded; patients who were vaccinated against SARS-CoV-2 presented vaccination certificates; patients also had to declare smoking status.

Table 1. Groups' characteristics.

Groups' characteristics	**ASTHMA + COVID-19 S1 (35 patients)**	**COPD + COVID-19 S2 (37 patients)**
Gender		
Female	21 (60%)	11 (29.73%)
Male	14 (40%)	26 (70.27%)
Age		
30-39 years	6 (17.14%)	1 (2.7%)
40-49 years	11 (31.43%)	6 (16.27%)
50-59 years	7 (20%)	7 (18.92%)
60-69 years	5 (14.29%)	11 (29.73%)
70-79 years	4 (11.43%)	8 (21.62%)
>80 years	2 (5.71%)	4 (10.81%)
Environments origins		
Urban	19 (54.29%)	23 (62.16%)
Rural	16 (45.71%)	14 (37.84%)
Smokers	24 (68.57%)	29 (78.38%)
Vaccinated	19 (54.29%)	11 (29.73%)

Applied tests

We processed the necessary information about each patient from the medical records.

At the time of discharge, all patients were asked about their symptoms.

The symptoms were represented by:

- fatigue;
- cough;
- dyspnea;
- cognitive and mental disorders;
- palpitations;
- taste and smell dysfunctions;
- headaches.

After discharge, patients were included in the pulmonary rehabilitation program, being evaluated at 3 and 6 months.

Patients with moderate or severe forms of COVID-19 have had a chest computed tomography (CT).

First computed tomography was performed during hospitalization, and the following scan performed 3 or/and 6 months depending of patient's evolution.

The most common aspects on CT of COVID-19 are represented by: ground glass opacities, consolidation, reticular pattern, and crazy paving pattern.

These aspects correlate with the evolution and degree of severity of COVID-19.

Severe forms of COVID-19 have had a slow healing of lesions after the rehabilitation program. (Figure 1a and Figure 1b)

Figure 1a. Severe form of COVID-19.

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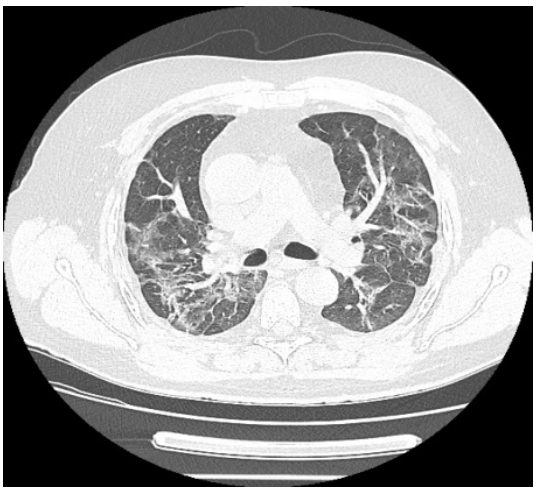

Figure 1b. After 6 months.

After being included in the respiratory rehabilitation program, most patients with moderate forms of COVID-19 had a marked regression of lung lesions. (Figure 2a, Figure 2b. and Figure 2c.)

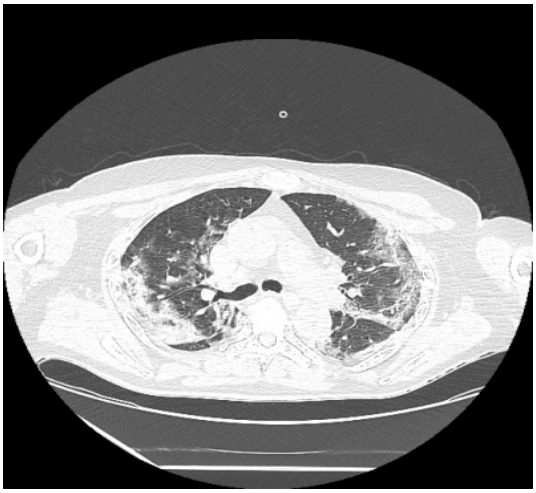

Figure 2a. Moderate form of COVID-19.

Figure 2b. After 3 months.

Figure 2c. After 6 months.

To evaluate patients before and after inclusion in the medical rehabilitation program, we used:

- Six-Minute Walk Distance (6MWD):

This test is a simple clinical test, easy to perform, well tolerated by patients.

It measures the distance in meters traveled by a patient during a 6 minutes interval [12].

The patient should wear loose clothes, appropriate shoes, avoid heavy meals and physical exercises before performing the test.

In this context, the test helped us to assess the increase in exercise capacity and the improvement of dyspnea.

- Patient Specific Functional Scale:

Was required for evaluating the perception of limitations in performing daily activities.

Patients were asked to identify up to 5 activities that they could not perform as before.

They assessed on a scale of 11 points the level of difficulty, where 0 means unable to perform and 10 able to perform the activity.

- Monitoring parameters: oxygen saturation of arterial blood, heart rate, respiratory rate, blood pressure.
- Borg Scale-for quantifying dyspnea.

Patients received information about their health and education regarding self-management strategies, symptoms control, and rehabilitation interventions.

The pulmonary rehabilitation program was personalized as stated by forbearance of the patients, functional deficits and comorbidities present.

The exercises were performed daily, with a gradual increase in intensity.

A submaximal intensity leads to the failure of the rehabilitation program.

The intensity of the effort should be practiced as close as possible to the maximum performance of the patient.

The objectives of the rehabilitation program were to:

- reduce the intensity of dyspnea;
- increase muscle strength;
- recover to mobility;
- improve exercise capacity;
- reduce anxiety and prevents depression;
- promote a balanced diet with proper nutrition;
- reduce pulmonary fibrosis lesions;
- reduce the number of hospitalizations for obstructive ventilatory dysfunction;
- increase the quality of life.

The basic components of pulmonary rehabilitation were:

1. Patient education-smoking cessation, vaccination against SARS-CoV-2 infection, use of inhalation devices for obstructive ventilatory dysfunction, self-management strategies.
2. Kinetic measures:

- Respiratory rehabilitation-forced exhalation and postural drainage were performed to promote the elimination of bronchial secretions.
- Muscle training-The training consists of exercises for each muscle group with an increase in the number of repetitions every 2-3 days depending on the patient's results.

This training is an important part of lung rehabilitation, which addresses the respiratory muscles and peripheral muscles.

- Aerobic exercise: walking, jogging, treadmill running, ergonomic cycling, starting fromexercises with a low degree of difficulty to complex exercises, repeated several times per week, 30 minutes for each session.

1. Nutritional support-recommendation by a nutritionist of a diet appropriate to the patient's needs.
2. Psychological support-is a basic component of the medical rehabilitation program, being necessary to help the patient to adapt to the current situation.

It has been shown to reduce the patient's anxiety, depression and general condition.

Statistical processing

Statistical data were processed with the Data Analysis module of the Microsoft Excel program.

Statistical correlations were performed using the Fischer test, where a p-value <0.05 was considered statistically significant.

The results were represented by tables and diagrams.

Results

From the total of 72 patients included in our research, 35 of the patients were previously diagnosed with asthma-S1(49%) and 37 of the patients were previously diagnosed with COPD-S2 (51%).

In group S1 women predominated, and in group S2 men predominated.

In the general group forms of COVID-19 were: mild forms-14 patients (19%), moderate forms-36 patients (50%) and severe forms-22 patients (31%).

Patients in group S1 had more mild forms of COVID-19 compared to patients in group S2-9 of the 35 subjects with asthma compared with 5 of the 37 subjects with COPD.

Patients in group S1 also had more moderate forms-19 of the 35 patients compared to patients in group S2-17 of the 37 patients.

The most severe forms of COVID-19 were in group S2-15 of 37 patients compared to patients in group S1-7 of the 35 patients (Figure 3).

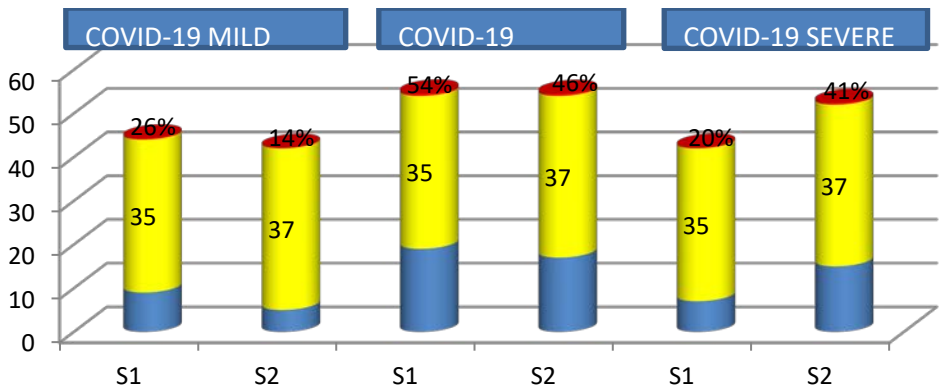

Figure 3. Severity of COVID-19 forms.

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Smoking was statistically significantly correlated with the severity of COVID-19 and aggravated obstructive ventilatory dysfunction (p=0,0415).

Thus, 20 of the 22 patients (91%) diagnosed with severe forms of COVID-19 are smokers and only 3 of the 14 patients (21%) with mild forms are smokers.

Unvaccinated patients predominated in our study, 40 of the 72 patients (56%) refused outpatient vaccination.

All participants of the study with mild forms of COVID-19 were vaccinated.16 of the 36(44%) patients with moderate forms were vaccinated.

All severe forms of COVID-19 occured in unvaccinated patients. Of the 14 patients with mild form of COVID-19, 9 were in group S1 and 5 were in group S2.

Of the 16 patients vaccinated with moderate form of COVID-19, 10 were in group S1 and 6 patients were in group S2 (Figure 4).

Vaccination was statistically significantly correlated with mild forms of the disease compared to severe forms (p=0,0001).

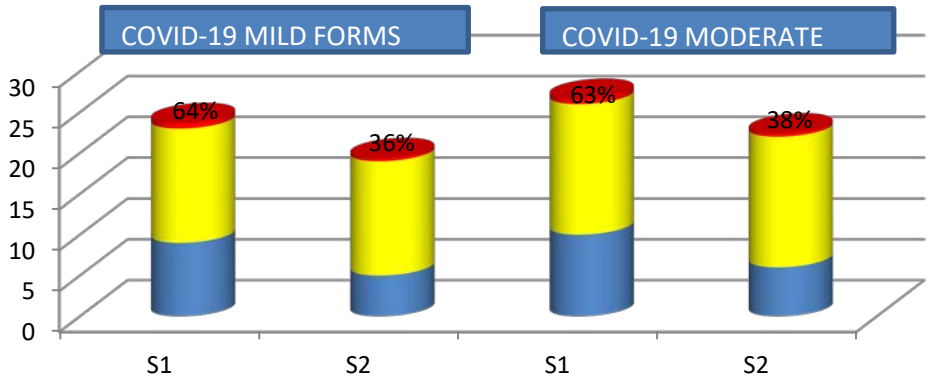

Figure 4. The benefits of vaccination.

Patients showed various symptoms at discharge.

The most common symptom was fatigue, which was seen in 50 of the 72 patients included in the study.

The cough was present in 40 of the 72 patients, and it was a dry cough, residual cough.

Dyspnea was found in 29 of the patients, cognitive and mental disorders in 25 of the patients, palpitations in 19 of the patients, dysfunctions of taste and smell in 18 of the patients, and headaches in 10 of the patients (Figure 5).

Patients may experience more symptoms on discharge.

Mild forms of COVID-19 were associated with taste and smell dysfunctions, and moderate and severe forms with cognitive and mental disorders.

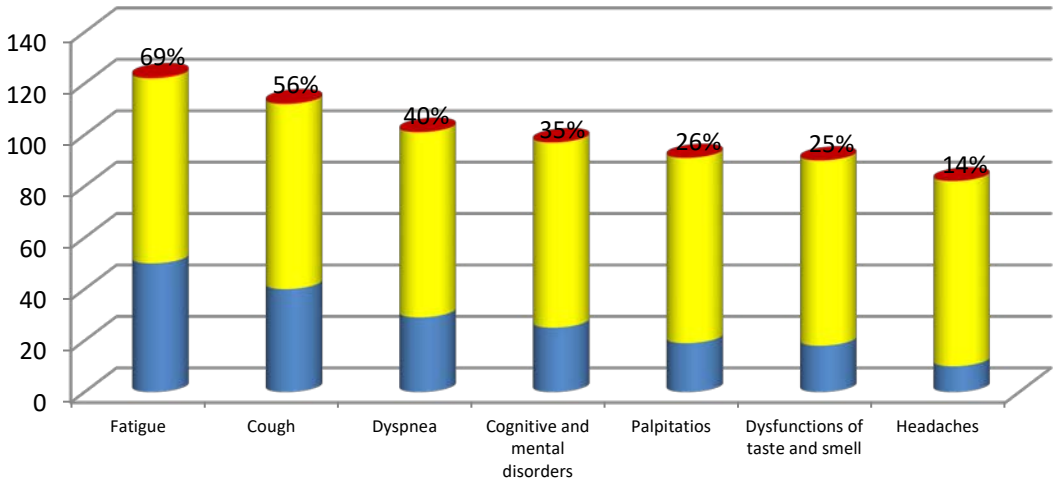

Figure 5. Discharge symptoms.

After being included in the rehabilitation program, patients performed the exercises daily or several times a week, depending on tolerance.

At the end of the rehabilitation program sessions, all patients had a favorable clinical course.

We assessed the increase in exercise tolerance through the 6-minute walking test (6MWD).

Among patients with mild forms of COVID-19 all patients in group S1 showed increased exercise tolerance and most patients in group S2-4 of the 5 patients.

Of the patients diagnosed with moderate forms of COVID-19, 14 of 19 subjects in the S1 lot and 10 of the 17 subjects in the S2 lot showed a 6-minute improvement in the walking test.

Even patients diagnosed with severe forms of COVID-19 showed increased exercise tolerance, 4 of 7 patients in group S1 and 7 of the 15 patients in group S2 (Figure 6).

Absolute contraindications:

- recent myocardial infarction;
- recently diagnosed unstable angina pectoris;

Relative contraindications:

- resting heart rate>120 beats per minute;
- blood pressure >180/100mmHg;

Increased exercise tolerance, improved dyspnea, and increased oxygen saturation were present in all patients after the end of the pulmonary rehabilitation program.

There was a difference between mild forms of COVID-19, where patients after 6 months showed only taste and smell disorders, while those with severe forms of COVID-19 had a much slower favorable clinical course.

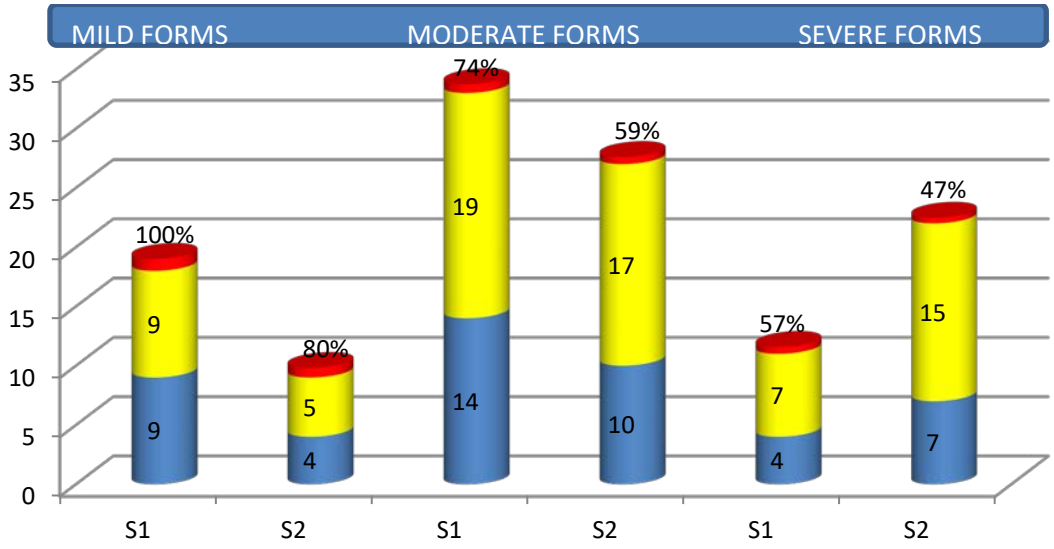

Figure 6. Effort tolerance (6MWD).

Patients received at the time of discharge, but also after 6 months of pulmonary rehabilitation a questionnaire that assesses the ability to perform daily activities (Patient specific functional scale).

After the end of the sessions within the pulmonary rehabilitation program, a significant improvement of the daily activities was observed, even in the case of patients with severe forms.

In the case of subjects with mild forms, all patients in group S1 compared to 3 of the 5 patients in group S2 showed an increase in the number of points after completing the questionnaire after 6 months of rehabilitation.

Among patients with moderate forms of COVID-19, 16 patients in the S1 group had an improved functional scale compared to 13 patients in the S2 group.

Patients with severe forms of COVID-19, also presented better scores after completing the exercises in the rehabilitation program-5 of the 7 patients in S1 compared to 9 of the 15 patients in S2 (Figure 7).

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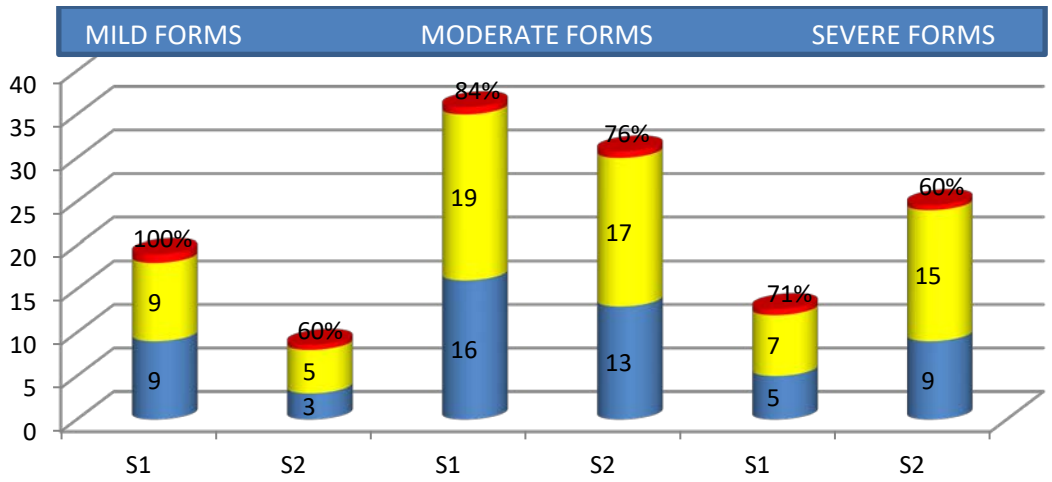

Figure 7. Patient Specific Functional Scale.

Discussion

Existing programs who are included in pulmonary rehabilitation could be used in the standard treatment for patients who have COVID-19 and show symptoms and changes in physical function, since the benefits of rehabilitation have been proven.

Pulmonary rehabilitation is mainly based on physical training, being necessary after the period of hospitalization, where the patient is inactive and spends a lot of time in bed [13].

As our study revealed that patients with COPD have a higher risk of evolving severe forms of COVID-19, a review study found that COPD was found to be notably correlated with severe forms of infection (OR: 5.69 [95:CI: 2.49-13.00], $I^2 = 0.0\%$, Cochran's Q, $p = 0.95$) [14].

The link between asthma and COVID-19 is controversial at this time.

In our study, patients diagnosed with asthma had more mild forms and fewer severe forms of COVID-19 compared to patients with COPD.

There are several contradictory results regarding the reported prevalence of asthma.

These differences, both regionally and nationally, could be explained by the fact that the influence of the outbreak of COVID-19 had a different effect in the regions [15].

It should be noted that in China, following epidemiological reports, asthma was not identified as a risk factor for patients infected with SARS-CoV-2, so it was underreported or there were no patients diagnosed with asthma and COVID-19 [16].

Another study was a prospective follow-up of the cohort was conducted between March 15 and April 15, 2020 at Bicêtre Hospital, University of Paris-Saclay, France which had 768 hospitalized patients, 37 (4.8%) presented in the antecedent's personal pathological diagnosis of asthma, confirmed in most cases by the pulmonologist-85%.

None of them presented with an asthma exacerbation[17].

However, there are also cases where asthma was specified as a comorbidity in patients who were hospitalized for SARS-CoV-2 infection, for example in the UK Biobank cohort of 269,070 subjects [18].

A systematic review of the literature that measured the prevalence and mortality risk of patients with pre-existing diseases before SARS-CoV-2 infection identified asthma as one of the important risk factors in patients with COVID-19[19].

As we demonstrated in our study, vaccination against SARS-CoV-2 infection is effective.

All people with mild forms of COVID-19 have been vaccinated.

The only supposed way to end the COVID-19 pandemic is mass vaccination of the population.

Even if some people are reluctant, two of the vaccines have proven effective in preventing SARS-CoV-2 infection and the occurrence of severe forms, a fact proven by two phase 3 clinical studies.

The most important measure that any individual can take is the vaccination[20].

For both groups in our study (S1 and S2) smoking was a risk factor for moderate and severe forms of the disease.

Smoking was statistically significantly correlated with the severity of COVID-19 and aggravated obstructive ventilatory dysfunction (p=0,0415).

The same was demonstrated in a systematic review based on five clinical trials, where Vardavas and Nikitara showed that smokers were 1.4 times more likely to have severe symptoms of COVID-19 and approximately 2.4 times more likely to be addmited to an intensive care unit [21].

As our study showed that respiratory rehabilitation had a positive impact on all forms of COVID-19, several studies around the world have shown this.

Another study carried out in France, in two departments specialized in rehabilitation demonstrated that the most frequent symptoms were dyspnea (n=35 (90%)) and fatigue (n=30 (77%)), relatively similar to our study-fatigue =69%, dyspnea=40%.

During rehabilitation, dyspnea, hyperventilation, 6MWT and quality of life improved significantly [22].

Also, a study conducted in Austria demonstrated the increase in exercise tolerance and the improvement of physical capacity, measured by an average increase of 6MWT by 176 (SD±137) meters on 23 patients released after a severe forms of COVID-19, who were included in an individualized, multidisciplinary rehabilitation program [23].

The common parameter followed in these studies was the 6MWD, with similar results as in our study, so that the increase in walking distance showed an increase in exercise tolerance after inclusion in the rehabilitation program.

The originality of our study was the use patient specific functional scale.

After discharge, patients had difficulty performing daily activities.

After completing the rehabilitation program, patients awarded more points than initially for their daily activities.

This demonstrates the beneficial effect of rehabilitation.

As we have demonstrated the importance of the rehabilitation program and another study performed in hospitals in Italy (Bari, Lumezzane, Tradate, Pavia and Veruno) in important departaments for respiratory rehabilitation demonstrated that pulmonary rehabilitation is practicable and successful in subjects recuperating from COVID-19, even for those in intensive care units [24].

Conclusions

1. Patients with COPD are increase risk to develop severe forms of COVID-19.

2. Smoking is an important risk factor for SARS-CoV-2 infection and obstructive ventilatory dysfunction.

3. Vaccination against SARS-CoV-2 infection is effective, being associated with mild forms of COVID-19.

4. Pulmonary rehabilitation is a key point in the management of patients with COVID-19, improving exercise capacity, reducing dyspnea, improving health, increasing oxygen saturation and quality of life.

Conflicts of interest

No conflicts of interests.

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Corresponding Author: Brînduș Gabriela-Marina, PhD Student, Doctoral School, University of Medicine and Pharmacy of Craiova, No 2-4, Petru Rareș Str. Craiova, 200349, Romania, e-mail: gabriela.brindus@yahoo.com