Respiratory Medicine 190 (2021) 106679

Contents lists available at ScienceDirect

Respiratory Medicine

journal homepage: www.elsevier.com/locate/rmed

Respiratory muscle training program supplemented by a cell-phone application in COPD patients with severe airflow limitation

Barata Paula Irina [a], Marc Monica Steluta [b,*], Tudorache Emanuela [b], Manolescu Diana [c], Olar Dana Cristina [a], Frandes Mirela [d], Oancea Cristian [b]

[a] *"Vasile Goldis" University of Arad, Faculty of Medicine, Department of Physiology, Arad, Romania*
[b] *University of Medicine and Pharmacy "Victor Babes" Timisoara, Department of Pulmonology, Timisoara, Romania*
[c] *University of Medicine and Pharmacy "Victor Babes" Timisoara, Radiology Department, Timisoara, Romania*
[d] *University of Medicine and Pharmacy "Victor Babes" Timisoara, Department of Biostatistics and Medical Informatics, Timisoara, Romania*

ARTICLE INFO

Keywords:
Rehabilitation
Inspiratory muscle
COPD

ABSTRACT

Purpose: The purpose of this study was to implement a respiratory muscle training program through a mobile phone application for COPD patients with severe airflow limitation.
Methods: We conducted an experimental study to determine the efficacy of a six-month mobile phone application. At least three times a week for six months the patients would participate in an online training session. We evaluated the lung volumes, maximal inspiratory and expiratory pressure (MIP/MEP) and diaphragm amplitude. The tests were performed at the beginning and at the end of the study.
Results: Thirty-four patients with severe COPD, aged between 44 and 67 years (Mean ± SD, 59.29 ± 6.063), accepted to follow a rehabilitation program based on the use of the Pneumocontrol application. We observed on increased of MEP from the pre-rehabilitation state (83.41 cmH2O) to the post-rehabilitation state (95.03 cmH2O), z = 5.087, $p < 0.001$. Also, the median MIP significantly increased from the pre-rehabilitation state to the post-rehabilitation state, z = 5.052, $p < 0.001$. Diaphragmatic distance also increased from 2.81 cm to 3.44 cm, z = 5.069, $p < 0.001$.
Conclusion: Respiratory muscle training supplemented through a cell phone-based application can improve respiratory muscle strength and diaphragm mobility.

1. Introduction

Affecting more than 5% of the general population, chronic obstructive pulmonary disease (COPD) represents an economic and healthcare burden worldwide. Its prevalence is on the rise and constitutes one of the leading causes of death in developed countries [1].

It is well known that COPD is a multi-systemic disease that affects different organs and systems [2]. The diaphragm muscle is affected by this disease due to both airway obstruction and pulmonary hyperinflation. Pulmonary hyperinflation decreases the operating length of the diaphragm leading to a change in shape and amplitude. Therefore, patients with COPD have inspiratory muscle weakness [2]. Moreover, pulmonary hyperinflation reduces the performance of the diaphragm to generate pressure and flow, thus resulting in a decreased diaphragmatic excursion [3].

Exercise training is the cornerstone of pulmonary rehabilitation in patients with COPD. Reports show that pulmonary rehabilitation programs with exercise training improve quality of life, respiratory symptoms and exertional and overall dyspnea. Moreover, they decrease the need for hospitalisation [4]. Respiratory muscle training (RMT) generally includes both inspiratory (IMT) and expiratory (EMT) muscle training in a various extent. IMT has the most important role in this type of training and the role of EMT is still under debate [5]. The most used forms of RMT in patients with COPD are: breathing against resistive loading (RL), breathing against pressure threshold loading (PTL) and voluntary normocapnic hyperpnea (NH) [5].

Modern times have led to a paradigm shift in which hospital settings are being transferred to home care settings thus reducing healthcare resources. Furthermore, there is an increasing use of mobile phone applications and other technologies to support the change in the management of care [6].

In Europe, the majority of pulmonary rehabilitation programs are

* Corresponding author. Eftimie Murgu sq. 300310 Timisoara, Romania.
E-mail address: stel.marc@gmail.com (M.M. Steluta).

https://doi.org/10.1016/j.rmed.2021.106679
Received 13 July 2021; Received in revised form 13 September 2021; Accepted 30 October 2021
Available online 2 November 2021

hospital-based and rely on constant monitoring to achieve optimal benefits [7]. More and more exercise options appeared for the patient's benefit, from telemonitoring to mobile phone applications all to reduce health care costs and enhance pulmonary rehabilitation. In 2008, 90% of the US adult population used a cell phone [7]. Nguyen et al. observed that cell phones can, in the short term, provide effective behaviour change interventions [8]. The effect of these cell phone applications and tele-medicine in COPD patients are still at debate. Some meta-analyses and systematic reviews present positive results [9], but are not confirmed in other studies [10].

Searching the literature, we observed that for COPD patients very few studies have applied mobile phone applications to improve different outcomes. Therefore, the purpose of this study was to determine if respiratory muscle training provided through a mobile phone application can improve respiratory muscle strength in COPD patients with severe airflow limitation.

2. Material and methods

2.1. Study design

At least three times a week for six months patients performed online training sessions with a professional pulmonary rehabilitation physical therapist. We evaluated the lung volumes, maximal inspiratory and expiratory pressure (MIP/MEP) and diaphragm amplitude.

All the subjects have been informed upon the research, and informed consent was obtained before the beginning of the study. The study design and contract forms were approved by the Ethics Committee of the hospital (nr.4870/July 09, 2020).

2.1.1. Patients

We included in the study 49 patients with severe stable COPD. The subjects were classified according to the ATS/ERS criteria for the severity of airway obstruction [11]. The included individuals were chronic patients with COPD who came to the Pulmonary Rehabilitation Centre but could not perform in-hospital exercises due to the recent modifications caused by the pandemic. Exclusion criteria was: exacerbation in the last six months, comorbidities and acute states that could interfere with their current health condition, use of medication that could affect exercise responses, musculoskeletal conditions and impaired vision affecting the subject's ability to follow the mobile phone application. During the six months period, 13 patients did not follow the protocol by skipping the exercises programs and 2 patients had exacerbation thus at the end of the study, 34 patients remained. The first evaluation was performed in the first day when the patients were included in the study and the last evaluation was at the end of the study, after six months.

2.2. Outcome measures

2.2.1. Lung volumes

To determine the pulmonary volumes (spirometry) and maximal inspiratory and expiratory pressure we used the Smart PFT UI (Medical equipment Europe GmbH) device. Criteria for the included patients were according to the ATS/ERS guideline: history of smoking >20 packs/year, forced expiratory volume (FEV$_1$<80% predicted; FEV$_1$/forced vital capacity (FVC) < 0.7 predicted and physician diagnosis for COPD [11, 12].

2.2.2. Respiratory muscle strength

Maximal inspiratory pressure was determined by placing a nose clip on the patient that was instructed to expire to residual volume followed by maximum inspiration. To assess maximal expiratory pressure, the patient was instructed to breathe in until total lung capacity was reached, followed by a forced exhalation. Three assessments were recorded and the best value was used. All the manoeuvres were performed according to standard procedures [13].

2.2.3. Mobile phone application

Pneumocontrol is a mobile phone application specially developed by a group of pulmonology physicians together with an IT specialist for patients with COPD. Patient's first completed in the application the COPD assessment test. Depending on the score obtained from the questionnaire patients were classified as: normal evolution (continue treatment), alarming evolution (need for medical consultation), and immediate medical emergencies. Every patient was registered through the application in the physician's data base. The medical physician could verify daily the patient's status. The mobile application allows the patient identification through a user account. Values obtained from the questionnaire were automatically processed and the score indicated the patient classification according to the medical standards and disease control level [12].

The application has three specific areas: self-management plan with questionnaire, inhalation devices techniques with video presentation, and pulmonary rehabilitation exercises with video presentation and subtitles. All the patients received instructions on the functionalities of the application before starting the study. The application is easy to understand and compatible for all smart phones.

2.2.4. Diaphragmatic ultrasound assessment

Diaphragmatic breathing represents an important part of pulmonary rehabilitation. A ClearVue 550 machine (Philips Healthcare, Eindhoven, NL) equipped with a 2–5-MHz curve array (C5-2®) was used for this study to evaluate the diaphragm mobility. All patients were examined in the supine position with the arms elevated above the head in normal breathing. The supine position of the patient is preferred, because there is less overall variability, less side-to-side variability, and greater reproducibility [14]. The anterior subcostal view of the diaphragm dome movement was observed using the transducer placed between the midclavicular and anterior axillary line.

The excursion of right diaphragm was measured during quiet breathing at tidal volume (TV) using a convex probe of 3.5 MHz. Measurements of diaphragm kinetics were assessed in the M-mode technique. Only US measurements obtained at patients' right side were considered for statistical analysis, as left side offers a poor acoustic window in the majority of patients, as in previous studies [15].

2.3. Intervention

2.3.1. Inspiratory muscle training

For the respiratory muscle training, patients were instructed to perform daily training with respiratory muscle device (POWERbreathe MEDIC). This training modality of respiratory muscle training is commonly used in patients with COPD and is based on breathing against resistive loading. For this type of training, patients have to inhale or exhale through a variable-diameter orifice. The smaller the orifice the greater the load achieved.

Instruction on how to use the device was performed by a respiratory therapist and the device was calibrated for each patient at the beginning of the study. Compliance with the training program was performed at every session and exercises were corrected. The patients had to perform at each training sessions, 30 breaths through the device at a certain level that was determined for each subject. If the training session was too easy, patients were instructed to reduce de orifice and turn the device at a higher level thus increasing the breathing load. This procedure was repeated each time the patient inhaled lightly 30 times at that certain level.

2.3.2. Pneumocontrol application

The pulmonary rehabilitation section of the mobile phone application consisted of pulmonary rehabilitation programs recommended by the American Thoracic Society such as pursed lip breathing, diaphragmatic breathing, strength training with light weight and home based exercises for upper and lower extremity endurance training [16]. The pulmonary rehabilitation programs were performed online through the application with a specialised physical therapist to make sure that all the patients understood how to perform the exercises. A respiratory rehabilitation session generally lasted 45 min and followed the principle of accessibility where patients started with light and simple exercises and reached more complex exercises. Every session included breathing techniques, chest expansion exercises, weight training for upper and lower body muscles and aerobic exercises adapted so that every patient could perform them in their household. Airway clearance techniques were performed only if needed. Strength training was performed with weight and elastic bands. Each patient had their own weights according to their strength. Our goal for this type of training was between 8 and 12 repetitions [16]. Weights and elastic bands were changed when the patients considered the exercises to easy. All the training sessions were individualised according to the scores obtained from the questionnaire in the application and according to the patient's symptoms.

2.3.3. Statistical analysis

Data were analyzed using the SPSS v.20 software (SPSS Inc., Chicago, IL, USA). Continuous data with Gaussian distribution were presented as mean and standard deviations (SDs), while continuous variables without Gaussian distribution were described as median and interquartile range (IQR). The categorical data were presented as percentage (absolute frequency). The distribution of continuous data was tested for normality using the Shapiro–Wilk test and for equality of variances by using Levene's test.

A related-samples Wilcoxon signed-rank test was conducted to determine the effect of using the mobile phone application-based rehabilitation program on the respiratory muscle strength. The correlation between studied variables was evaluated using Spearman's rank sum correlation coefficient (non-Gaussian distributed variables), its statistical significance being assessed using the t-distribution score test.

A p-value of 0.05 was considered as the threshold for statistical significance, and a confidence level of 0.95 was considered for estimating intervals.

3. Results

Thirty-four patients with severe COPD, aged between 44 and 67 years (Mean ± SD, 59.29 ± 6.063), accepted to follow a rehabilitation program based on the use of the *Pneumocontrol* application. For each patient, we measured both ponderal status and vital capacity. We observed that 11.4% patients were underweight, equal proportions of patients (35.3%) were at normal and overweight range, while 17.6% were obese (Class I Moderate). The characteristics of the patients are presented in Table 1.

Most of the patients presented moderate (47.1%) and severe (44.1%) COPD, according to FEV_1 (%) level. When considering the FEV1/FVC ratio, we observed that most of the patients (85.3%) presented severe COPD.

Of the thirty-four patients included in the study, using the Pneumocontrol application elicited an improvement in respiratory muscle strength in thirty-three participants compared to the pre-rehabilitation state, whereas at one patient we saw no improvement. This patient was underweight, aged 55 years, and presented severe COPD according to the ATS statements [12].

Considering the MEP values, we observed that all the patients improved their respiratory muscle strength after using the application. Regarding the diaphragmatic amplitude, using the Pneumocontrol application generated an improvement in respiratory muscle strength in thirty-three participants compared to the pre-rehabilitation state, whereas at one participant we saw no improvement. This patient had the same characteristics as the previously described patient.

We observed a statistically significant median increase in the parameters describing the respiratory muscle strength. More exactly, we observed an increase of MEP from the pre-rehabilitation state (83.41 cmH2O, IQR = 64.34–95.03) to the post-rehabilitation state (95.03 cmH2O IQR = 80.45–107.58), Wilcoxon signed-rank test z = 5.087, $p < 0.001$. Also, the median MIP significantly increased from the pre-rehabilitation state to the post-rehabilitation state, Wilcoxon signed-rank test z = 5.052, $p < 0.001$. Moreover, the diaphragmatic distance also increased from 2.81 cm (IQR = 2.11–3.27) to 3.44 cm (IQR = 2.98–3.97), Wilcoxon signed-rank test z = 5.069, $p < 0.001$. The comparative results of respiratory muscle strength before vs. after rehabilitation are presented in Table 2.

A graphical representation of both MIP pre-rehabilitation and MIP post-rehabilitation is presented in Fig. 1. We can observe that the median value of MIP pre-rehabilitation is significantly lower than median value of MIP post-rehabilitation.

Also, a comparative representation of MEP pre-rehabilitation vs. MEP post-rehabilitation is presented in Fig. 2. We can observe that the median value of MEP pre-rehabilitation is significantly lower than median value of MEP post-rehabilitation.

The respiratory muscle strength was evaluated measuring both MIP and MEP, as well as the diaphragmatic distance (DD) before and after the rehabilitation program. The comparative representation of DD pre-rehabilitation vs. DD post-rehabilitation is included in Fig. 3. We can see that the median value of DD pre-rehabilitation is significantly lower than median value of DD post-rehabilitation.

Diaphragm mobility before rehabilitation was positively significantly associated with inspiratory muscle strength and positively associated with expiratory muscle strength before rehabilitation, Spearman's $r = 0.484$, $p = 0.004$, and Spearman's $r = 0.320$, $p = 0.065$, respectively. Also, the diaphragm mobility after rehabilitation was

Table 1
Patients characteristics.

Parameter	Min	Max	Mean ± SD	95% CI for mean	
				Lower	Higher
Age (years)	44	67	59.29 ± 6.063	57.18	61.41
BMI (kg/m^2)	17	33.7	25.106 ± 4.78	23.44	26.77
Lung functions					
FVC (L)	1.77	3.58	2.51 ± 0.38	2.38	2.64
FVC (%)	52	89	61.79 ± 7.83	59.06	64.52
FEV_1 (L)	0.51	1.53	0.96 ± 0.21	0.89	1.03
FEV_1 (%)	21	39	29.88 ± 4.77	28.22	31.55
FEV_1/FVC (%)	28	57	40.65 ± 7.88	37.9	43.4

Notes: Continuous variables (with gaussian distribution) are indicated by their mean and standard deviations.
Abbreviations: BMI, body mass index; FVC, forced vital capacity; FEV_1, forced expiratory volume in the first second.

Table 2
Respiratory muscle strength before vs. after rehabilitation.

Parameter[a]	Pre-rehabilitation	Post-rehabilitation	p-value[b]
MEP (cmH2O)	83.41 (64.34–95.03)	95.03 (80.45–107.58)	<0.001
MEP (%)	68.70 (59.40–81.50)	79.20 (71.70–93.40)	<0.001
MIP (cmH2O)	57.91 (43.43–79.74)	73.21 (60.26–93.40)	<0.001
MIP (%)	53.60 (40.10–70.90)	67.75 (56.30–86.70)	<0.001
Diaphragmatic distance (cm)	2.81 (2.11–3.27)	3.44 (2.98–3.97)	<0.001

Notes: [a]Continuous variables (without Gaussian distribution) are indicated by their median (interquartile range). [b]p-value was computed using the related-samples Wilcoxon Signed- Ranked test.
Abbreviations: MEP, maximal expiratory pressure; MIP, maximal inspiratory pressure.

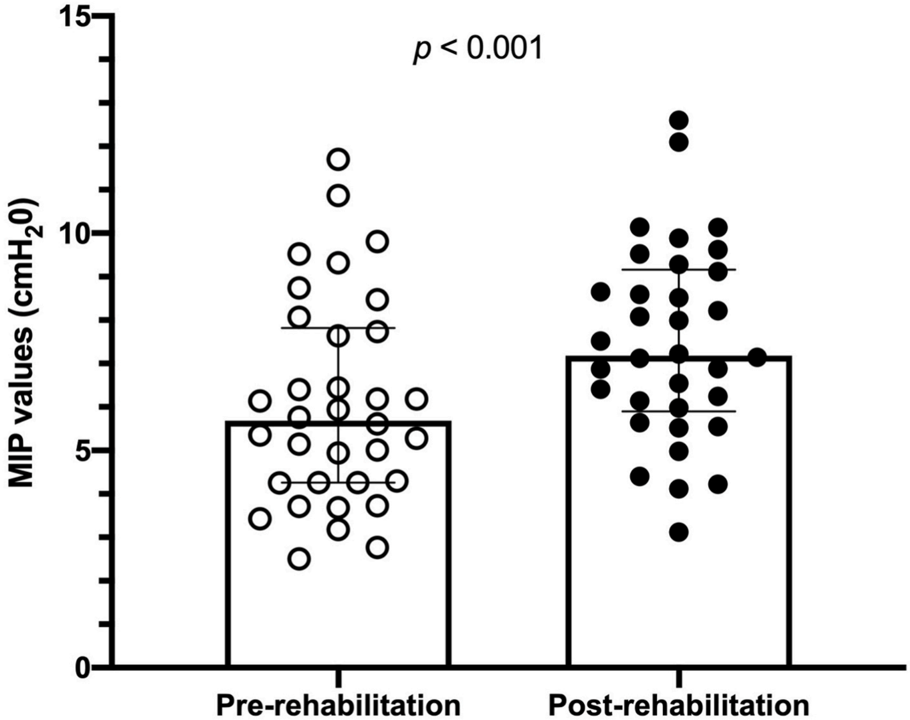

Fig. 1. Comparative representation of MIP (maximal inspiratory pressure) individual values, median and interquartile range before vs. after rehabilitation program.

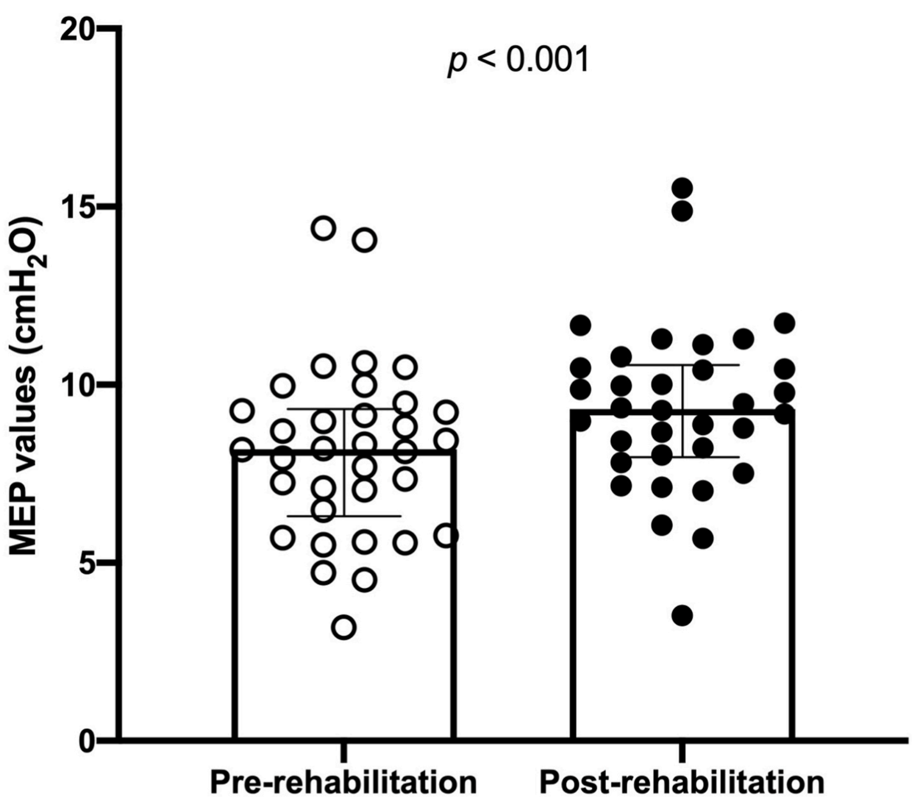

Fig. 2. Comparative representation of MEP (maximal expiratory pressure) individual values, median and interquartile range before vs. after rehabilitation program.

positively significantly associated with inspiratory muscle strength and positively associated with expiratory muscle strength after rehabilitation, Spearman's $r = 0.421$, $p = 0.013$, and Spearman's $r = 0.144$, $p = 0.417$, respectively.

4. Discussion

The importance of recovering the diaphragm's mobility and strength is not only for alleviating symptoms but also related to survival in COPD patients [17]. Diaphragm function is largely assessed in these patients

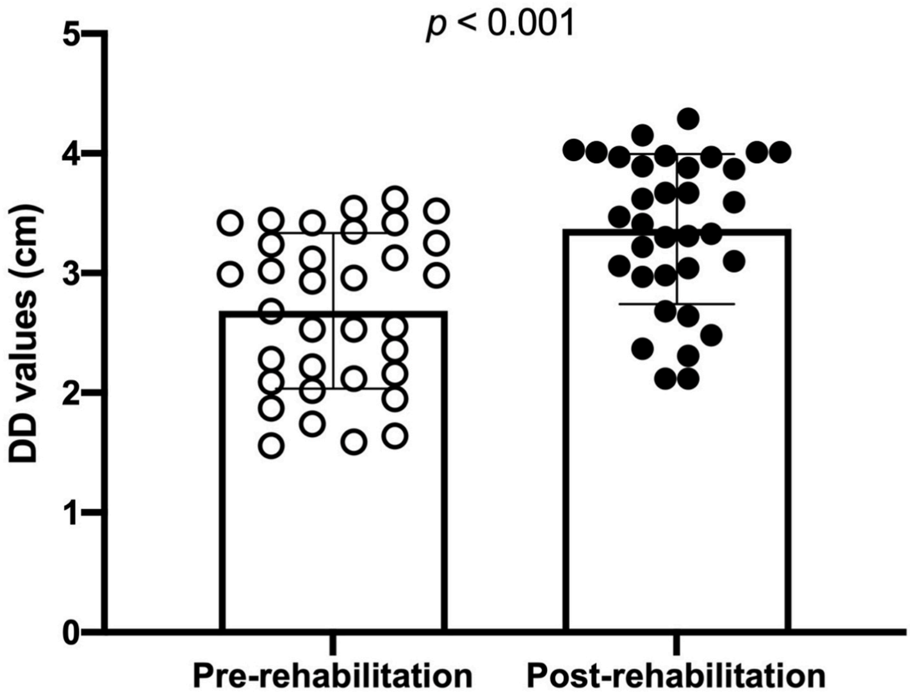

Fig. 3. Comparative representation of DD (diaphragmatic distance) individual values, median and interquartile range before vs. after rehabilitation program.

and it has been demonstrated that inspiratory muscle weakness is related to dyspnea and reduced quality of life [18].

Previous studies have demonstrated that pulmonary rehabilitation can improve the strength of inspiratory muscles in COPD patients [3, 17].

This study assumed that exercises delivered through a mobile phone application can improve diaphragm mobility and inspiratory muscle strength. Our data showed that reduced diaphragm mobility is associated with lower inspiratory and expiratory muscle strength.

We demonstrated that under the assistance of a mobile phone application, COPD patients were able to perform specific pulmonary rehabilitation exercises in a home-based program. The adherence to exercises was monitored in real-time on the website and reinforced by reminders when the patient missed performing their training.

Previous studies reported different methods to measure diaphragm mobility under various radiologic techniques. Singh et al. used two-dimensional chest radiograms [19] others described chest wall movement and diaphragm length using computed tomography and dynamic magnetic resonance imaging [20,21].

These methods are costly and affect the subjects with high radiation exposure. In our study, diaphragmatic mobility was evaluated during rest breathing by M-mode ultrasonography because of its advantages (safety, feasibility, repeatability and reproducibility) [22].

We observed that diaphragmatic mobility has improved significantly after six months of using the mobile phone application with specific exercise programs.

The majority of the pulmonary rehabilitation programs are executed in the hospital and they usually last for 4–12 weeks. In order to achieve optimal physiological benefits, patients should exercise at least three times per week [23]. It has been shown that regular returns to the hospital and patients motivation and compliance are important limiting factors [24].

The fact that home-based rehabilitation programs are preferred by patients, several methods have been developed with proven clinical benefits in quality of life and exercise tolerance [25]. Due to the web-based reminders and frequent respiratory symptoms assessment we observed that our cell phone application can prove efficient home-based exercises. Our findings are similar to those of W-T Liu et al. who included 24 patients that performed endurance walking from a program installed on a cell phone [26].

Mi Chun et al. observed on a group of 117 COPD patients a significant improvement, over 1 cm, in the mobility of the diaphragm after pulmonary rehabilitation. In his study, patients were observed for more than a 12 week run-in period and continued their exercises daily at home [3]. Similar to his study we recorded a significant improvement of the diaphragm mobility, but our patients did not benefit from rehabilitation training in a medical centre.

A study that has split its COPD patients into two groups, one that had markedly improved after pulmonary rehabilitation and one that only slightly improved, emphasized the utility of diaphragmatic ultrasound assessment and its correlation with PR outcomes. The authors showed that US assessment of diaphragmatic function can accurately identify COPD patients who meaningfully improved after PR [27].

We observed a positive relationship between diaphragm mobility and inspiratory muscle strength. Our findings can be explained by the fact that air trapping makes the inspiratory muscle to work in a shortened position thus affecting the potential of contraction [28]. Our findings are similar to those of Rocha et al. who evaluated the diaphragmatic mobility in relation to lung function, respiratory muscle strength, dyspnea and physical activity in daily life in patients with COPD [29].

Another author found that inspiratory muscle training improved diaphragmatic mobility in patients following cardiac surgery [30]. These findings suggest a relationship between improved diaphragmatic mobility and inspiratory muscle strength.

Taking into consideration all the above mentioned, it is clear that lower diaphragmatic mobility in patients with COPD has a potential to impair inspiratory and expiratory muscle strength.

One of the limitations of this study is the small size and self-selected nature of the included patients. It is clear that the patients who completed the study were highly motivated. Larger cohorts and sections of COPD population are needed to confirm the findings of this study. Another limitation would be that we did not have a control group with in-hospital pulmonary rehabilitation. Due to ethical reasons, we considered that all COPD patients that could perform pulmonary rehabilitation should benefit of this application. Due to the fact that COPD is inversely related to socioeconomic status and mostly affect older adults, our studied population had a mean age of 59, this might be a limitation and should be taken into consideration. This could also be a reason why 13 out of 49 patients did not comply to the exercise program.

5. Conclusion

Respiratory muscle training supplemented through a cell phone application can improve respiratory muscle strength and diaphragmatic mobility. Moreover, ultrasound assessment could be used as an additional tool for evaluation of clinical effects of pulmonary rehabilitation in patients with COPD.

Ethical approval and consent to participate

All the subjects have been informed upon the research, and informed consent was obtained before the beginning of the study. The study design and contract forms were approved by the Ethics Committee of the Infectious Diseases and Pneumology hospital "Dr. Victor Babes" (nr.4870/July 09, 2020).

Consent to participate

Written informed consent was obtained before the beginning of the study, from all the subjects.

Availability of data and materials

The authors confirm that all data underlying the findings are fully available without restriction. Data can be obtained after submitting a request to the hospital.

Funding

No funding was received for this work.

Authors' contributions

BPI, MMS, TE conceived of the presented idea, MD, FM, ODC, wrote the manuscript with support from CO, BPI, MMS and FM and TE performed the calculations. MD performed the ultrasound assessment. All authors discussed the results and contributed to the final manuscript.

CRediT authorship contribution statement

Barata Paula Irina: conceived of the presented idea. **Marc Monica Steluta:** conceived of the presented idea, performed the calculations. **Tudorache Emanuela:** conceived of the presented idea, performed the calculations. **Manolescu Diana:** performed the ultrasound assessment, wrote the manuscript with support from Oancea Cristian, Barata Paula Irina, Marc Monica Steluta. **Olar Dana Cristina:** wrote the manuscript with support from Oancea Cristian, Barata Paula Irina, Marc Monica Steluta. **Frandes Mirela:** wrote the manuscript with support from. **Oancea Cristian:** Barata Paula Irina, All authors discussed the results and contributed to the final manuscript.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Acknowledgements

The authors would like to thank Dr. PT. Crisan Alexandru Florian for the physical therapy programs and respiratory muscle evaluations.

References

[1] Global Strategy for the Diagnosis, Management, and Prevention of Chronic Obstructive Pulmonary Disease, 2019, 2019 Report.
[2] F. Laghi, M.J. Tobin, Disorders of the respiratory muscles, Am. J. Respir. Crit. Care Med. 168 (1) (2003) 10–48, https://doi.org/10.1164/rccm.2206020.
[3] E.M. Chun, S.J. Han, H.N. Modi, Analysis of diaphragmatic movement before and after pulmonary rehabilitation using fluoroscopy imaging in patients with COPD, Int J COPD 10 (2015) 193–199, https://doi.org/10.2147/COPD.S74438.
[4] D. Verrill, C. Barton, W. Beasley, W.M. Lippard, The effects of short-term and long-term pulmonary rehabilitation on functional capacity, perceived dyspnea, and quality of life, Chest 128 (2) (2005) 673–683, https://doi.org/10.1378/chest.128.2.673.
[5] E. Crisafulli, S. Costi, L.M. Fabbri, E.M. Clini, Respiratory muscles training in COPD patients, Int. J. Chronic Obstr. Pulm. Dis. 2 (1) (2007) 19–25, https://doi.org/10.2147/copd.2007.2.1.19.
[6] L. Nici, R. ZuWallack, An official American thoracic society workshop report: the integrated care of the COPD patient, Proc. Am. Thorac. Soc. 9 (1) (2012) 9–18, https://doi.org/10.1513/pats.201201-014ST.
[7] R.A. Sansone, L.A. Sansone, Cell phones: the psychosocial risks, Innov Clin Neurosci 10 (1) (2013) 33–37.
[8] H.Q. Nguyen, D.P. Gill, S. Wolpin, B.G. Steele, J.O. Benditt, Pilot study of a cell phone-based exercise persistence intervention post-rehabilitation for COPD, Int. J. Chronic Obstr. Pulm. Dis. 4 (2009) 301–313.
[9] S. Lundell, Å. Holmner, B. Rehn, A. Nyberg, K. Wadell, Telehealthcare in COPD: a systematic review and meta-analysis on physical outcomes and dyspnea, Respir. Med. 109 (1) (2015) 11–26, https://doi.org/10.1016/j.rmed.2014.10.008.
[10] M. Chatwin, G. Hawkins, L. Panicchia, et al., Randomised crossover trial of telemonitoring in chronic respiratory patients (TeleCRAFT trial), Thorax 71 (4) (2016) 305–311, https://doi.org/10.1136/thoraxjnl-2015-207045.
[11] B.L. Graham, I. Steenbruggen, M.R. Miller, et al., Standardization of spirometry 2019 update. An official American thoracic society and European respiratory society technical statement, Am. J. Respir. Crit. Care Med. 200 (8) (2019) e70–e88, https://doi.org/10.1164/rccm.201908-1590ST.
[12] K.F. Rabe, S. Hurd, A. Anzueto, et al., Global strategy for the diagnosis, management, and prevention of chronic obstructive pulmonary disease: GOLD executive summary, Am. J. Respir. Crit. Care Med. 176 (6) (2007) 532–555, https://doi.org/10.1164/rccm.200703-456SO.
[13] P. Laveneziana, A. Albuquerque, A. Aliverti, et al., ERS statement on respiratory muscle testing at rest and during exercise, Eur. Respir. J. 53 (6) (2019) 1801214, https://doi.org/10.1183/13993003.01214-2018.
[14] E.O. Gerscovich, M. Cronan, J.P. McGahan, K. Jain, C.D. Jones, C. McDonald, Ultrasonographic evaluation of diaphragmatic motion, J. Ultrasound Med. 20 (6) (2001) 597–604, https://doi.org/10.7863/jum.2001.20.6.597.
[15] M.J. Tobin, F. Laghi, L. Brochard, Role of the respiratory muscles in acute respiratory failure of COPD: lessons from weaning failure, J. Appl. Physiol. 107 (3) (2009) 962–970, https://doi.org/10.1152/japplphysiol.00165.2009.
[16] C.L. Rochester, I. Vogiatzis, A.E. Holland, et al., An official American Thoracic Society/European Respiratory Society policy statement: enhancing implementation, use, and delivery of pulmonary rehabilitation, Am. J. Respir. Crit. Care Med. 192 (11) (2015) 1373–1386, https://doi.org/10.1164/rccm.201510-1966ST.
[17] R. Nussbaum, C. Kelly, E. Quinby, A. Mac, B. Parmanto, B.E. Dicianno, Systematic review of mobile health applications in rehabilitation, Arch. Phys. Med. Rehabil. 100 (1) (2019) 115–127, https://doi.org/10.1016/j.apmr.2018.07.439.
[18] P.V. Santana, ALP de Albuquerque, Respiratory muscles in COPD: be aware of the diaphragm, J. Bras. Pneumol. 44 (1) (2018) 1–2, https://doi.org/10.1590/s1806-37562018000010001.
[19] B. Singh, P.R. Eastwood, K.E. Finucane, Volume displaced by diaphragm motion in emphysema, J. Appl. Physiol. 91 (5) (2001) 1913–1923, https://doi.org/10.1152/jappl.2001.91.5.1913.
[20] N. Pettiaux, M. Cassart, M. Paiva, M. Estenne, Three-dimensional reconstruction of human diaphragm with the use of spiral computed tomography, J. Appl. Physiol. 82 (3) (1997) 998–1002, https://doi.org/10.1152/jappl.1997.82.3.998.
[21] D.K. McKenzie, R.B. Gorman, J. Tolman, N.B. Pride, S.C. Gandevia, Estimation of diaphragm length in patients with severe chronic obstructive pulmonary disease, Respir. Physiol. 123 (3) (2000) 225–234, https://doi.org/10.1016/s0034-5687(00)00172-9.
[22] A. Testa, G. Soldati, R. Giannuzzi, S. Berardi, G. Portale, N. Gentiloni Silveri, Ultrasound M-mode assessment of diaphragmatic kinetics by anterior transverse scanning in healthy subjects, Ultrasound Med. Biol. 37 (1) (2011) 44–52, https://doi.org/10.1016/j.ultrasmedbio.2010.10.004.
[23] P.I. Pedro, L. Maia Santos, C. Braco Forte, A. Dias, C. Cruz, F. Rodrigues, Benefits of pulmonary rehabilitation in patients with chronic obstructive pulmonary disease and interstitial lung disease with the same dyspnea severity, Pulmonology 25 (2) (2019) 117–118, https://doi.org/10.1016/j.pulmoe.2019.01.002.
[24] A.E. Holland, A. Mahal, C.J. Hill, et al., Home-based rehabilitation for COPD using minimal resources: a randomised, controlled equivalence trial, Thorax 72 (1) (2017), https://doi.org/10.1136/thoraxjnl-2016-208514, 57 LP - 65.
[25] M.R. Güell, P De Lucas, B. Gáldiz, et al., Home vs hospital-based pulmonary rehabilitation for patients with chronic obstructive pulmonary disease, A Spanish Multicenter Trial 44 (10) (2008) 6–12.
[26] W. Liu, C. Wang, H. Lin, et al., Efficacy of a Cell Phone-Based Exercise Programme for COPD, 2008, pp. 651–659, https://doi.org/10.1183/09031936.00104407.
[27] C. Crimi, E. Heffler, T. Augelletti, et al., Utility of ultrasound assessment of diaphragmatic function before and after pulmonary rehabilitation in COPD

patients, Int J COPD 13 (2018) 3131–3139, https://doi.org/10.2147/COPD.S171134.
[28] H.W. Kang, T.O. Kim, B.R. Lee, et al., Influence of diaphragmatic mobility on hypercapnia in patients with chronic obstructive pulmonary disease, J. Kor. Med. Sci. 26 (9) (2011) 1209–1213, https://doi.org/10.3346/jkms.2011.26.9.1209.
[29] F.R. Rocha, A.K.V. Brüggemann, D. de S. Francisco, CS de Medeiros, D. Rosal, E. Paulin, Diaphragmatic mobility: relationship with lung function, respiratory muscle strength, dyspnea, and physical activity in daily life in patients with COPD, J. Bras. Pneumol. 43 (1) (2017) 32–37, https://doi.org/10.1590/s1806-37562016000000097.
[30] M. Kodric, R. Trevisan, C. Torregiani, et al., Inspiratory muscle training for diaphragm dysfunction after cardiac surgery, J. Thorac. Cardiovasc. Surg. 145 (3) (2013) 819–823, https://doi.org/10.1016/j.jtcvs.2012.07.087.