

Physical therapy in chronic obstructive pulmonary disease (analysis of the evidence-based medicine)

DOI: <https://doi.org/10.5114/pq.2018.75993>

Kateryna Tymruk-Skoropad, Lyubov Tsizh, Bogdan Vynogradskyi, Iuliia Pavlova

Lviv State University of Physical Culture, Lviv, Ukraine

Abstract

Introduction. The purpose of the study is to present the forms of rehabilitation used in chronic obstructive pulmonary disease (COPD) in various centres. Widespread occurrence of COPD, significant disability, high treatment costs, permanently increasing and more profound knowledge about the pathogenesis and course of COPD lead to a comprehensive study of respiratory rehabilitation and physical therapy of the disease.

Methods. The selected databases were Cochrane Library, Medline, PubMed, Embase. Clinical trials were analysed from the ClinicalTrials.gov database. The search was performed on July 20, 2017, with the following search terms: 'COPD,' 'COPD exercises,' 'COPD rehabilitation,' 'COPD physical activity,' 'COPD physical therapy.'

Results. The share of the research on exercises for COPD cases amounts to 20% of the total number of publications (1984 references). The largest number of COPD studies proved to come from the PubMed database. In 2012, this number made up 3588 entries (135% increase over the previous 10 years).

Conclusions. In evidence-based medicine databases, in the total number of the published research results pertaining to COPD, the proportion of studies on rehabilitation makes up 9.8–15.95%, and that of physical therapy constitutes 3.8–11.5%. Taking into consideration the conclusions of systematic reviews with reference to the key role of rehabilitation and physical therapy in the COPD patients' treatment, close attention should be focused currently on the identification of indispensable components of respiratory rehabilitation and the evaluation of its efficacy.

Key words: physical therapy, COPD, chronic obstructive pulmonary disease, clinical research, respiratory rehabilitation

Introduction

Chronic diseases remain the major cause of mortality throughout the world, accounting for 60% of the death rate in total. As much as 80% of the mortality rate from chronic diseases refers to low and average income countries. Besides, chronic diseases present a heavy economic burden, hindering the development of many countries [1, 2].

Chronic obstructive pulmonary disease (COPD) occupies one of the leading positions in the health care system. In 2012, more than 3 million people died of COPD, accounting for almost 6% of the mortality rate in the world that year. According to WHO estimations, COPD in a moderate and severe form has affected 65 million people. It is anticipated that by 2030, COPD might be the third most significant cause of mortality in the world [3].

As of 2015 in Ukraine, the prevalence of COPD was at least 7%, which amounted to 3 million persons [4].

COPD prevalence, significant disability, death rate, and economic losses associated with the disease stipulate considerable attention of scientists and practitioners in this area. Physical therapy is one of the most indispensable constituents of COPD patients' treatment [5]. Therefore, the search for the most efficient respiratory rehabilitation means and programs, as well as the investigation of its acute and long-term effect never cease.

Any new trend in medical science and practice should rely on certain provisions whose objectivity should give no rise

to doubt [6, 7]. Consideration of evidence-based medicine data, specialized systematic reviews that filter the entire flow of information and provide a physical therapist with the available data about the efficacy of certain techniques at a particular stage should be regarded as a significant information source that allows to diagnose the disease properly and promptly, as well as to select the most efficient method of patients' rehabilitation [8, 9].

Thus, physical therapy should also be guided by the evidence-based medicine for research substantiations, for further elaboration of new rehabilitation techniques and improvement of the existing means, modalities and methods, for theoretical and methodological support of rehabilitation interventions.

For many years, COPD has remained on the list of priority diseases in the health care system of Ukraine to meet the current and future needs of the patients [10]. Rehabilitation care for COPD cases demands close attention accordingly.

The purpose of the study is to present the forms of rehabilitation used in COPD in various centres.

Subjects and methods

The evidence-based medicine databases of Cochrane Library, Medline, PubMed, and Embase have been analysed. Current clinical trials were investigated from the ClinicalTrials.gov database.

The available data search was accomplished by exam-

Correspondence address: address: Iuliia Pavlova, Lviv State University of Physical Culture, Kostyushko Str., 11, Lviv, Ukraine, 79007, e-mail: paviova.j.o@gmail.com

Received: 2018.01.30

Accepted: 2018.03.12

Citation: Tymruk-Skoropad K, Tsizh L, Vynogradskyi B, Paviova I. Physical therapy in chronic obstructive pulmonary disease (analysis of the evidence-based medicine). *Physiotherapy Quarterly*. 2018;26(2):1–8; doi: <https://doi.org/10.5114/pq.2018.75993>.

ining the publication title, key words, or summary. The search terms were as follows: 'COPD,' 'COPD exercises,' 'COPD rehabilitation,' 'COPD physical activity,' 'COPD physical therapy.'

When it was possible, we eliminated publications on irrelevant areas, systematic reviews of literature, non-human subject papers, and texts not reported in the English language.

The search was performed on July 20, 2017.

Ethical approval

The conducted research is not related to either human or animal use.

Results

The urgency of the research on a variety of issues of COPD etiopathogenesis, treatment, and rehabilitation, as well as the provision of comprehensive support to COPD patients remains to be quite pressing.

As of July 2017, the Cochrane Central Register of Controlled Trials had registered 9891 publications on COPD (Table 1). The share of the research on exercises for COPD cases amounts to 20% of the total number of publications (1984 references) (Figure 1).

There are more references to the search term 'COPD rehabilitation' than the key words 'COPD physical therapy'

(9.8% of the total share of COPD publications with the 'COPD rehabilitation' term against 3.8% for 'COPD physical therapy'). This might be due to the content of the terms themselves, as well as the practical meaning of rehabilitation and physical therapy in COPD patients. Rehabilitation presents itself as a broader concept and the programs of pulmonary (respiratory) rehabilitation include exercises (physical therapy) as a key component. Besides, certain programs of respiratory rehabilitation contain other interventions, like examination, education, control, psychological support, and dietary recommendations. Respiratory rehabilitation is considered to be one of the most essential approaches to COPD treatment, and its integral part is physical therapy [11].

The share of the reviews on rehabilitation analysis in the Cochrane Database of Systematic Reviews equals 10% of all the reviews on COPD; that of reviews on physical therapy amounts to 5.9%, and that for COPD exercises is 35%.

The Medline database contains 427 references pertaining to scientific studies on various COPD issues. The share of publications with the key words of 'exercises,' 'rehabilitation,' 'physical activity,' and 'physical therapy' amounts to 18%, 15.9%, 15.9%, and 11.5%, correspondingly.

The largest number of COPD studies were found in the PubMed database. Since 1992, a steady growth in the number of publications on COPD could be observed. If in 1992 the

Table 1. The quantity of scientific research on COPD in evidence-based medicine databases of the world and the libraries of Ukraine

	Number of publications by the retrieval term				
	COPD	COPD exercises	COPD rehabilitation	COPD physical activity	COPD physical therapy
Cochrane Central Register of Controlled Trials	9891	1984	978	372	380
Cochrane Database of Systematic Reviews	117	42	12	8	7
Medline	427	77	68	68	49
PubMed	71,481	6870	5871	7092	3159
Embase	2480	524	336	210	140
Abstract database of the Vernadsky National Library of Ukraine	456	-	3	1	1

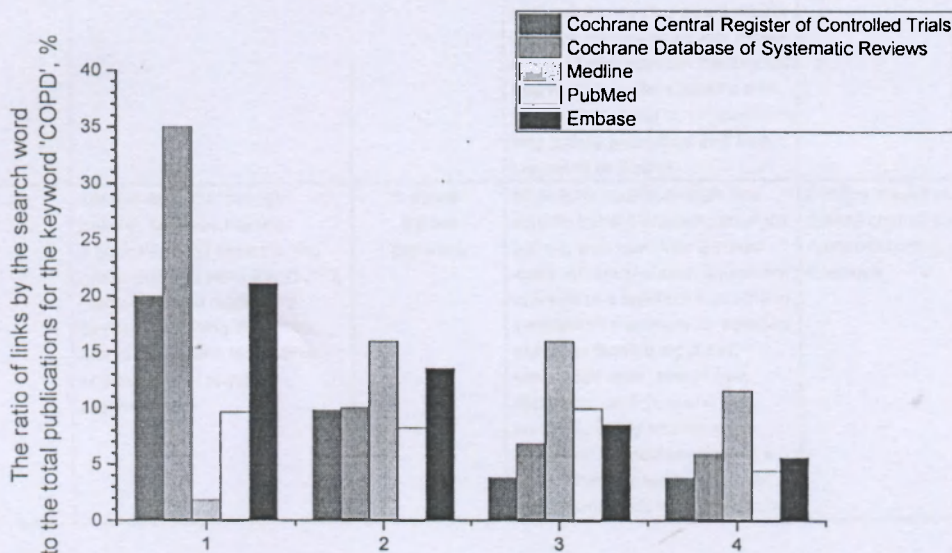


Figure 1. The ratio of search results in the scientifically proven databases by the defined key words to the total number of publications on COPD: 1 – 'COPD exercises,' 2 – 'COPD rehabilitation,' 3 – 'COPD physical activity,' 4 – 'COPD physical therapy'

Table 2. Summary of the studies included in the review (n = 19)

	Author, year [reference]	Sample (number of subjects with COPD)	Type of PR	Duration; frequency	Applied load	Main results
1	Langer et al., 2015 [18]	25	Mechanical threshold loading (MTL) devices; electronic tapered flow resistive loading (TFRL) device	8 weeks; 2-per-day training	Each training included 30 breaths (3–5 min per lesson) with the highest tolerable intensity	Endurance capacity of inspiratory muscles in the TFRL group was higher than in the MTL group
2	Grosbois et al., 2015 [12]	211	Home-based PR according individual action plan (warm-up; strengthening exercises; stretching; balance exercises)	8 weeks; 5 times per week	3 daily upper and lower limb muscle strengthening exercises were systematically proposed (with instructions sheets), for 10–15 min per day, using weights and dumbbells (0.5 or 1 kg) and/or Elastiband® elastic bands. Each exercise comprised a series of 10 repeated movements	Home-based PR was effective in terms of exercise capacity, anxiety and depression, and quality of life in short term, medium term (6 months), and long term (12 months)
3	Do Nascimento et al., 2015 [13]	14	Home-based PR (warm up; aerobic activity; stretching; relaxation)	2 months; 3 times per week	Aerobic exercise consisted of walking for 40 min with an intensity of 85% of the maximum speed achieved in the Incremental Shuttle Walk Test. Resistance exercises for the upper limbs in primitive diagonal, with load determined on the basis of the incremental testing of the upper limbs	Improvement in exercise tolerance; increased inspiratory muscle strength; improved health-related quality of life; control of systemic inflammation
4	Liao et al., 2015 [19]	61*	Upper-limb exercise training; pursed lip breathing; treadmill exercises; airway clearance (such as chest percussion and postural drainage); smoking cessation; health education; self-health management	4 days; 2-per-day training (30–40 min)	NP	The rehabilitation program reduced the symptoms of COPD (dyspnoea, cough, sputum expectoration)
5	Camillo et al., 2016 [29]	423*	Social, nutritional, and psychological support; optimization of medical treatment; physical training	6 months; 3 trainings per week + 3 months non obligatory; 2 trainings per week	Months 1–3: intensive program; months 4–6: support program	Higher 5-year survival in patients with COPD
6	He et al., 2015 [14]	94*	Exercise (stretches, endurance, and strength training); relaxation; breathing retraining; health education	From the 2 nd day of hospitalization to discharge from hospital; 2 times per day (30 min)	Lower-limb endurance training was performed on a treadmill with the initial workload prescribed at 60% of the peak work; upper-limb endurance training comprised repetitive bilateral shoulder flexion and abduction using a light weight and was synchronized with expiration for 2 min; strength training with free weights or the subject's own body weight (1 set of 10 repetitions was initially prescribed and then increased to 3 sets)	Increasing quality of life and daily activity
7	Santos et al., 2015 [15]	34	Aerobic exercise; strength training; flexibility training; 5 education and skills training group-oriented sessions (COPD, medication and respiratory devices, breathing exercises, bronchial hygiene techniques, and benefits of physical exercise)	8 weeks; 3 times per week	60 or 80% maximum work rate aerobic training intensity; strength training was combined 2 times/week with multi-station equipment in 3 sets of 8 repetitions at 50% of 1-repetition maximum for selected exercises (seated leg press, seated calf raise, seated row, abdominal crunch, and chest press); flexibility training was combined 3 times/week with 5 s of stretching for each of the 7 selected large body muscle exercises	Positive impact on COPD patient-centred outcomes, symptom control, and exercise tolerance

8	Valenza et al., 2017 [16]	36	Home-based PR program (controlled breathing training, aerobic exercise with elastic bands, neuromuscular electrical stimulation)	8 weeks; 2 hours per week	10 min of control breathing training, 30 min of neuromuscular electrical stimulation, and 5 min of relaxation	Improved cardiorespiratory performance and functionality
9	MacMillan et al., 2017 [28]	15	Eccentric cycling; concentric cycling	10 weeks; three 30-min sessions per week	The target cycling power was 60–80% peak work rate achieved during the baseline incremental cardiopulmonary exercise test	Improvement of strength, muscle mass, and composition of the locomotor apparatus
10	Houchen-Wolloff et al., 2018 [30]	1515	Endurance-based walking; muscle strength training for the upper and lower extremities	7 weeks; 2 times per week (2-hour sessions)	At a level equating to 85% of predicted peak maximal oxygen uptake (VO_2)	Increased survival
11	Katajisto and Laitinen, 2017 [31]	75	Aerobic exercise; muscle strength training for the upper and lower extremities; educational lectures	6–8 weeks; 3 times per week (two 105-min sessions + 1 independent lesson)	NP	The number of hospital days were reduced by 54%
12	Zainuldin et al., 2016 [32]	93	Aerobic and strength training; walking exercise	2 weeks; twice a day physiotherapy exercise sessions + therapy sessions + counselling session	Each exercise session consisted of 30 min of aerobic and strength training, with at least 10 min spent in walking exercise. Walking exercise intensity was prescribed as 80% of the average speed achieved in the 6-min walking test	Significant improvements in exercise capacity, health; reduced 30-day readmission rate
13	Abd El-Kader et al., 2016 [27]	100	Aerobic exercise or resistant exercise training	12 weeks; aerobic exercises 3 times per week (40-min sessions) or resistant training 3 times per week (60-min sessions)	Treadmill aerobic exercise (60–70% of maximum heart rate); resistance exercises (70–85% of 1 resistance maximum)	Aerobic exercises modulated inflammatory cytokine levels
14	Leite et al., 2015 [20]	16	Treadmill exercises	12 weeks; 3 times per week	4 weeks at 60% of the peak velocity reached in the incremental test ($v\text{VO}_{2\text{peak}}$) (50 min of continuous effort), followed by 4 weeks of sessions at 75% of $v\text{VO}_{2\text{peak}}$ (30 min of continuous effort), and 4 weeks of interval training (5 × 3-min effort at $v\text{VO}_{2\text{peak}}$, separated by 1 min of passive recovery)	Positive effect on autonomic modulation and aerobic power
15	Aquino et al., 2016 [21]	28	High-intensity aerobic training (treadmill exercises) or high-intensity aerobic training combined with resistance training (combined training, treadmill exercises + resistance exercises)	4 weeks; 10 times per week (30-min sessions)	Treadmill exercises with the following progression (70–90% maximum heart rate); resistance training with the following progression (exercises for deltoids, quadriceps, biceps, and dorsal muscles; 70–90% 1 repetition maximum 3 sets, 4–10 repetitions)	improving of neurocognitive functioning with the combined training protocol
16	Santus et al., 2016 [25]	250	Ergometric load; 1 session of exercises with strengthening of the upper and lower extremities; breathing exercises; training of inspiratory muscles; methods of bronchial cleansing and coughing optimization	3 weeks (± 3 days); 6–7 times per week	The intensity of the ergometric load set at 60–80% of the maximum workload based on the results of 6-min walking test, and increased during the PR program in accordance with the improvement of the patient. Exercise for strengthening of the upper and lower extremities and breathing exercises (30 min a day, 6 days a week); training of inspiratory muscles (20 min per day, 7 days a week); methods of bronchial cleansing and coughing optimization (30 min twice daily, 7 days a week)	Positive effect on diffusing capacity for carbon monoxide

17	Xi et al., 2015 [26]	60	Health education program; respiratory training program	12 months	Abdominal breathing (diaphragmatic breathing) was performed for 10 min twice per day in the morning, and was increased in terms of the lasting time of the exercise until it became the normal method for breathing throughout the day; upper limb exercises (beginning with the duration of 5 min and gradually increasing to 20 min); lower limb exercises (10 min per day and gradually increasing up to 20 min each day)	Lung function was improved, the degeneration of lung function was delayed, the general prognosis was improved
18	Mehani, 2017 [22]	40	Inspiratory or expiratory muscle training	2 months; 3 times per week	Inspiratory training with an intensity of 15–60% of the maximal inspiratory pressure; expiratory training with an equal intensity, adjusted to the maximal expiratory pressure	Significant improvement in forced vital capacity, forced expiratory volume in the first second, blood gases (SaO ₂ %, PaO ₂ , PaCO ₂ , and HCO ₃) in the 6-min walking distance
19	Basso-Vanelli et al., 2016 [23]	25	Physical training; inspiratory muscle training; calisthenics-and-breathing exercises	4 months; 3 times a week	Treadmill exercise (80% of the speed, inclination obtained in the exercise treadmill test); lower limb (flexor and extensor group) resistance exercises performed with free weights, with increases of 1–2 kg every 2 weeks depending on subject tolerance; the training of the inspiratory muscles carried out by PowerBreathe; the calisthenics-and-breathing program (series of 9 exercises, each performed 15 times)	Increase of thoracoabdominal mobility, physical exercise capacity; decreased dyspnoea on exertion

* patients with COPD exacerbation

COPD – chronic obstructive pulmonary disease, MTL – mechanical threshold loading, NP – not present, PR – physical rehabilitation, TFRL – tapered flow resistive loading

resource registered 565 references, in 2002 the number of references grew to 3588 (169% increase over 10 years); in 2012 this number reached 3588 entries (135% increase over 10 years). In 2016, PubMed already registered 4762 entries, which is 32% more than in 2012. Throughout the years, the ratio of the research devoted to COPD rehabilitation and physical therapy remained practically at the same level and amounted to an average of 9.6% and 4.5% of all the publications on COPD, respectively.

Such a thorough attention of the scientists to the issues of physical therapy, exercises, physical activity, and rehabilitation in general, among all the studies on COPD, confirms the crucial part of these concerns in the patients' treatment and denotes the relevance of the research in this area.

Unfortunately, the search in the abstract database of the Vernadsky National Library of Ukraine revealed only 3 references by 'COPD rehabilitation' search words, which is 0.7% of the 456 references by 'COPD' search word.

All studies found that pulmonary rehabilitation programs or individual physical therapy programs were effective in improving the quality of life [12–17], physical endurance [12–16, 18–23], respiratory muscle strength [13, 18, 23], reducing symptoms of COPD [14, 16, 19, 23], improving the function of external breathing [16, 24–26], blood parameters [22, 27], cognitive functions [21], functional state of muscles [28], survival rates [29, 30], and reducing the number of hospital days [31]. The main part of investigations was devoted to the comparison of therapeutic rehabilitation programs that included several components and referred to stable patients with COPD. Only a few studies considered the effects of individual interventions of the physical therapy arsenal [20–22,

24, 27] and the effectiveness of pulmonary rehabilitation in a hospital environment at COPD exacerbation [17, 19, 31, 32] (Table 2).

Discussion

The Cochrane Airways Group contains 2 systematic reviews on pulmonary rehabilitation in COPD (first published on February 23, 2015) [11] and pulmonary rehabilitation after COPD exacerbation (first published on December 8, 2016) [33]. To compare the effect of pulmonary rehabilitation and ordinary nursing upon the quality of life, as well as on the functional and maximum physical capacity, the authors of the first systematic review analysed 65 randomized controlled studies that involved the total of 3822 participants. The review confirmed a clinically significant reduction of dyspnoea and fatigue, increase of physical capacity, and improvement of the emotional sphere when applying pulmonary rehabilitation for at least 4 weeks. It was mentioned that rehabilitation was an indispensable component of COPD control, and further investigations comparing the effect of pulmonary rehabilitation versus traditional nursing are considered unwarranted. According to the authors, identifying necessary components of pulmonary rehabilitation, their duration and location, the degree of control, the intensity of training, and persistence of the effect achieved seems to be a promising and significant subject of research in COPD rehabilitation.

Taking into account a great number of studies on COPD aetiology, pathogenesis, and treatment, the currently existing practical guidelines for COPD patients management are based on recommendations with a high degree of evidence

[34–36]. Practical regulations for COPD rehabilitation are no exception. The PEDro.org.au physiotherapy evidence database contains 8 practical guidelines, 5 of which give general recommendations for pulmonary rehabilitation of COPD patients, another 2 are dedicated to managing dyspnoea, and 1 protocol deals with non-pharmacologic airway clearance therapies in hospitalized patients (COPD cases included).

All the analysed protocols describe pulmonary rehabilitation as a variety of components and can include physical exercises, training, instructions on the use of different respiratory techniques, and psychosocial support [33]. Pulmonary rehabilitation is recommended to all stable patients with exercise limitation despite pharmacologic treatment and to patients who have recently been hospitalized for an acute exacerbation [37–39].

Aerobic training is the groundwork of pulmonary rehabilitation. It is recommended that both aerobic training and resistance training be prescribed to COPD patients [40, 41]. A program of exercise training of the muscles of ambulation and upper extremities, as well as weightlifting training is recommended as a mandatory component of pulmonary rehabilitation for COPD patients [37–39, 42, 43].

Although it has been proven that training of the inspiratory-respiratory muscles results in their strengthening and improves the results of the 6-min walking test and spirometry, mandatory inclusion of this component in rehabilitation program is not foreseen [38].

The duration of pulmonary rehabilitation programs in studies ranged from an average of 4 to 12 weeks. The longest of the research programs was a 12-month program with recommended self lessons 5 times a day [26]. The effectiveness of a 4-day therapeutic program under stationary conditions was investigated in patients with COPD exacerbation [19]. It is proved that even a short-term application of physical therapy in combination with smoking cessation contributes to the reduction of COPD symptoms and increases the efficacy of managing elderly patients with exacerbation. Unfortunately, there are not enough studies to compare the effectiveness of certain physical therapy products in patients with COPD during acute exacerbation. Using a variable set of survey methods in the study makes it difficult to compare the peculiarities of the effects of different programs of pulmonary rehabilitation for patients with COPD.

Unfortunately, all the practical guidelines that were analysed provide no solution to a set of challenges faced by physical therapy experts dealing with COPD patients – in particular, the kind of physical therapy tactics to be adhered to during the period of exacerbation and admission of COPD patients who respond to upper and lower extremities training or to weight and aerobic exercises with increased dyspnoea and aggravation of the disease; the criteria according to which the training of inspiratory muscles or other pulmonary rehabilitation components should be applied; at what stages of treatment they should be applied; what operational criteria or markers should be used to evaluate the efficacy of a physical therapy session. These issues, as well as many other ones, are going to be solved in the course of diverse scientific studies.

Thus, the comprehension of current world trends in research on COPD, taking into account the already existing and yet scheduled clinical trials, enables the selection of the most relevant research lines. With this end in view, the ClinicalTrials.gov database has been analysed for clinical trial protocols by specific search words. This particular database contains clinical trial protocols from 50 US states and 201 countries.

ClinicalTrials.gov does not contain information about all the clinical trials carried out in the USA and further afield; not all the studies are legally eligible for registration. However, the procedure of clinical trials which concern not only pharmacological means application is becoming more widespread. Accordingly, out of 2893 protocols in the ClinicalTrials.gov database (as of August 4, 2017), almost 6.2% (178 protocols) found by 'COPD' search word pertained to COPD rehabilitation; 9.8% (283 protocols) were detected by the 'COPD exercises' key words; 1.15% (33 protocols) included the 'COPD physical therapy' key words.

Thus, the percentage of clinical trials pertaining to rehabilitation, physical therapy, and COPD exercises is lower as compared with the available publications in the scientific evidential database. Out of the 33 protocols relating to physical therapy for COPD, 14 are in active status.

Eight protocols of clinical trials dealt with particular physiotherapeutic techniques, modalities, and devices. More than half of these protocols (5 out of 8) related to the evaluation of the techniques effectiveness for training inspiratory-expiratory muscles, as well as to drainage and electrostimulation. One study was designed to assess the digital health promotion instrument and the effect of ergotherapy upon the improvement of day-to-day life of COPD subjects. Five clinical trial protocols were devoted to the study of rehabilitation program effect on quality of life and prognostic indicators of mortality (6-min walking test, spirometry indices, BODE index, body mass index).

Four clinical trial protocols referred to rehabilitation influence and efficacy in the outpatient and hospital settings.

The major criteria for the effectiveness of intervention in most of the analysed planned clinical trial protocols were the level of life quality, dyspnoea perception index (Borg scale), and 6-min walking test. Certain studies additionally planned to evaluate forced expiratory volume in 1 s (FEV₁), body mass index, dynamometry, activity of daily living, and CO₂ partial pressure in the blood.

Conclusions

The urgency of the studies concerning various aspects of COPD has not diminished. In evidence-based medicine databases, in the total number of the published research results pertaining to COPD, the proportion of studies on rehabilitation makes up 9.8–15.95%, and that of physical therapy 3.8–11.5%.

Taking into consideration the conclusions of systematic reviews of the key role of rehabilitation and physical therapy in the COPD patients' treatment, close attention should be currently focused on identifying indispensable components of respiratory rehabilitation and evaluating its efficacy.

The studies which are still in the active phase according to the protocols registered in ClinicalTrials.gov database focus on assessing the effectiveness of rehabilitation comprehensive programs in the outpatient and inpatient settings, as well as certain physical therapy techniques (mainly with devices).

Further research should concentrate particularly on the elaboration, substantiation, as well as theoretical and methodological support of a COPD patients comprehensive rehabilitation program that would include efficient components for all levels of hospital and outpatient care. In addition, it is important to develop a physical rehabilitation program for severe COPD subjects in the period of acute condition, when they are unable to practice exercises with weights or cyclic exercises. No less significant issue is to see in proper perspective the efficacy and remote impact of the elaborated program.

Disclosure statement

No author has any financial interest or received any financial benefit from this research.

Conflict of interest

The authors state no conflict of interest.

References

1. Qureshi H, Sharafkhaneh A, Hanania NA. Chronic obstructive pulmonary disease exacerbations: latest evidence and clinical implications. *Ther Adv Chronic Dis*. 2014;5(5):212–227; doi: 10.1177/2040622314532862.
2. Global Initiative for Chronic Obstructive Lung Disease. Global strategy for diagnosis, management, and prevention of COPD – 2016. Available from: <http://goldcopd.org/global-strategy-diagnosis-management-prevention-copd-2016/>.
3. WHO. Chronic obstructive pulmonary disease (COPD). Available from: <http://www.who.int/respiratory/copd>.
4. COPD in Ukraine: problems and ways of their solving [in Ukrainian]. 2015. Available from: <http://health-ua.com/articles/3876>.
5. Vincent EE, Chaplin EJ, Williams JE, Harvey-Dunstan T, Greening NJ, Steiner MC, et al. Experiences of patients undergoing pulmonary rehabilitation during an exacerbation of chronic respiratory disease. *Chron Respir Dis*. 2017;14(3):298–308; doi: 10.1177/1479972317695812.
6. Rochester CL, Spruit MA. Maintaining the benefits of pulmonary rehabilitation. *The hoiv graii*. *Am J Respir Crit Care Med*. 2017;195(5):548–551; doi: 10.1164/rccm.201609-1925ED.
7. Vos T, Barber RM, Bell B, Bertozzi-Villa A, Biryukov S, Bolliger I, et al. (Global Burden of Disease Study 2013 Collaborators.) Global, regional, and national incidence, prevalence, and years lived with disability for 301 acute and chronic diseases and injuries in 188 countries, 1990–2013: a systematic analysis for the Global Burden of Disease Study 2013. *Lancet*. 2015;386(9995):743–800; doi: 10.1016/S0140-6736(15)60692-4.
8. Broderick J, Mc Grath C, Cullen K, Talbot D, Gilmor J, Baily-Scanlan M, et al. Effects of pulmonary rehabilitation on exercise capacity and disease impact in patients with chronic obstructive pulmonary disease and obesity. *Physiotherapy*. 2018;104(2):248–250; doi: 10.1016/j.physio.2017.08.002.
9. Spruit MA, Pitta F, McAuley E, ZuWallack RL, Nici L. Pulmonary rehabilitation and physical activity in patients with chronic obstructive pulmonary disease. *Am J Respir Crit Care Med*. 2015;192(8):924–933; doi: 10.1164/rccm.201505-0929CI.
10. Inventory of the priority illnesses, diseases, and conditions in Ukraine as for 2017–2018 [in Ukrainian]. Available from: <http://www.nplz.org.ua/NatListDrugs/DisList/Forms/AllItems.aspx>.
11. McCarthy B, Casey D, Devane D, Murphy K, Murphy E, Lacasse Y. Pulmonary rehabilitation for chronic obstructive pulmonary disease. *Cochrane Database Syst Rev*. 2015;23(2):CD003793; doi: 10.1002/14651858.CD003793.pub3.
12. Grosbois JM, Gicquello A, Langlois C, Le Rouzic O, Bart F, Wallaert B, et al. Long-term evaluation of home-based pulmonary rehabilitation in patients with COPD. *Int J Chron Obstruct Pulmon Dis*. 2015;10:2037–2044; doi: 10.2147/COPD.S90534.
13. Do Nascimento ESP, Sampaio LMM, Peixoto-Souza FS, Dias FD, Gomes ELFD, Greiffo FR, et al. Home-based pulmonary rehabilitation improves clinical features and systemic inflammation in chronic obstructive pulmonary disease patients. *Int J Chron Obstruct Pulmon Dis*. 2015;10:645–653; doi: 10.2147/COPD.S76216.
14. He M, Yu S, Wang L, Lv H, Qiu Z. Efficiency and safety of pulmonary rehabilitation in acute exacerbation of chronic obstructive pulmonary disease. *Med Sci Monit*. 2015; 21:806–812; doi: 10.12659/MSM.892769.
15. Santos C, Rodrigues F, Santos J, Morais L, Barbara C. Pulmonary rehabilitation in COPD: effect of 2 aerobic exercise intensities on subject-centered outcomes – a randomized controlled trial. *Respir Care*. 2015;60(11):1603–1609; doi: 10.4187/respcare.03663.
16. Vaienza MC, Torres-Sanchez I, López-López L, Cabrera-Martos I, Ortiz-Rubio A, Valenza-Demet G. Effects of home-based superimposed neuromuscular electrical stimulation in severe chronic obstructive pulmonary disease patients: a randomized controlled clinical trial. *Eur J Phys Rehabil Med*. 2017; doi: 10.23736/S1973-9087.17.04745-1.
17. López-García A, Souto-Camba S, Blanco-Aparicio M, Gonzalez-Doniz L, Saieta JL, Vereá-Hernando H. Effects of a muscular training program on chronic obstructive pulmonary disease patients with moderate or severe exacerbation antecedents. *Eur J Phys Rehabil Med*. 2016; 52(2):169–175.
18. Langer D, Charususin N, Jacome C, Hoffman M, McConnell A, Decramer M, et al. Efficacy of a novel method for inspiratory muscle training in people with chronic obstructive pulmonary disease. *Phys Ther*. 2015;95(9): 1264–1273; doi: 10.2522/ptj.20140245.
19. Liao LY, Chen KM, Chung WS, Chien JY. Efficacy of a respiratory rehabilitation exercise training package in hospitalized elderly patients with acute exacerbation of COPD: a randomized control trial. *Int J Chron Obstruct Pulmon Dis*. 2015;10:1703–1709; doi: 10.2147/COPD.S90673.
20. Leite MR, Ramos EM, Kalva-Filho CA, Freire AP, de Alencar Silva BS, Nicolino J, et al. Effects of 12 weeks of aerobic training on autonomic modulation, mucociliary clearance, and aerobic parameters in patients with COPD. *Int J Chron Obstruct Pulmon Dis*. 2015;10:2549–2557; doi: 10.2147/COPD.S81363.
21. Aquino G, Iuliano E, di Cagno A, Vardaro A, Fiorilli G, Moffa S, et al. Effects of combined training vs aerobic training on cognitive functions in COPD: a randomized controlled trial. *Int J Chron Obstruct Pulmon Dis*. 2016; 11:711–718; doi: 10.2147/COPD.S96663.
22. Mehani SHM. Comparative study of two different respiratory training protocols in elderly patients with chronic obstructive pulmonary disease. *Clin Interv Aging*. 2017; 12:1705–1715; doi: 10.2147/CIA.S145688.
23. Basso-Vanelli RP, Di Lorenzo VA, Labadessa IG, Regueiro EM, Jamami M, Gomes EL, et al. Effects of inspiratory muscle training and calisthenics-and-breathing exercises in COPD with and without respiratory muscle weakness. *Respir Care*. 2016;61(1):50–60; doi: 10.4187/respcare.03947.
24. Charususin N, Gosselink R, McConnell A, Demeyer H, Topaiovic M, Decramer M, et al. Inspiratory muscle training improves breathing pattern during exercise in COPD patients. *Eur Respir J*. 2016;47(4):1261–1264; doi: 10.1183/13993003.01574-2015.
25. Santos P, Radovanovic D, Baizano G, Pecchiari M, Racanelli R, Sarno N, et al. Improvements in lung diffusion

- capacity following pulmonary rehabilitation in COPD with and without ventilation inhomogeneity. *Respiration*. 2016;92(5):295–307; doi: 10.1159/000448847.
26. Xi F, Wang Z, Oi Y, Brightwell R, Roberts P, Stewart A, et al. Long-term effect of respiratory training for chronic obstructive pulmonary disease patients at an outpatient clinic: a randomised controlled trial. *Clin Transl Med*. 2015;4:31; doi: 10.1186/s40169-015-0073-2.
 27. Abd El-Kader SM, Al-Jiffri OH, Al-Shreef FM. Plasma inflammatory biomarkers response to aerobic versus resisted exercise training for chronic obstructive pulmonary disease patients. *Afr Health Sci*. 2016;16(2):507–515; doi: 10.4314/ahs.v16i2.19.
 28. MacMillan NJ, Kapchinsky S, Konokhova Y, Gouspillou G, de Sousa Sena R, Jagoe RT, et al. Eccentric ergometer training promotes locomotor muscle strength but not mitochondrial adaptation in patients with severe chronic obstructive pulmonary disease. *Front Physiol*. 2017;8:114; doi: 10.3389/fphys.2017.00114.
 29. Camiilo CA, Langer D, Osadnik CR, Pancini L, Demeyer H, Burtin C, et al. Survival after pulmonary rehabilitation in patients with COPD: impact of functional exercise capacity and its changes. *Int J Chron Obstruct Pulmon Dis*. 2016;11(1):2671–2679; doi: 10.2147/COPD.S113450.
 30. Houchen-Wollioff L, Williams JEA, Green RH, Woitmann G, Steiner MC, Sewell L, et al. Survival following pulmonary rehabilitation in patients with COPD: the effect of program completion and change in incremental shuttle walking test distance. *Int J Chron Obstruct Pulmon Dis*. 2018;13:37–44; doi: 10.2147/COPD.S143101.
 31. Katajisto M, Laitinen T. Estimating the effectiveness of pulmonary rehabilitation for COPD exacerbations: reduction of hospital inpatient days during the following year. *Int J Chron Obstruct Pulmon Dis*. 2017;12:2763–2769; doi: 10.2147/COPD.S144571.
 32. Zainuldin R, Sasiadek KM, Abdul Raub NA, Tay NW. An evaluation on the effects of inpatient pulmonary rehabilitation following acute exacerbation of chronic obstructive pulmonary disease in a Singapore hospital. *Ann Acad Med Singapore*. 2016;45(4):169–171.
 33. Puhan MA, Gimeno-Santos E, Scharplatz M, Troosters T, Walters EH, Steurer J. Pulmonary rehabilitation following exacerbations of chronic obstructive pulmonary disease. *Cochrane Database Syst Rev*. 2011;10:CD005305; doi: 10.1002/14651858.CD005305.pub3.
 34. Geinas CJ, Lewis CN, Harper M, Meizer B, Agar G, Roif JD, et al. Aerobic exercise training does not alter vascular structure and function in chronic obstructive pulmonary disease. *Exp Physiol*. 2017;102(11):1548–1560; doi: 10.1113/EP086379.
 35. Mesquita R, Meijer K, Pitta F, Azcuna H, Goertz YMJ, Essers JM, et al. Changes in physical activity and sedentary behaviour following pulmonary rehabilitation in patients with COPD. *Respir Med*. 2017;126:122–129; doi: 10.1016/j.rmed.2017.03.029.
 36. Salman Z, Nohari MM, Tybor D, Khan AB, Diab KJ. COPD: recent updates and role of chronic disease management and protocolized management. *Clin Pulm Med*. 2017; 24(4):170–175; doi: 10.1097/CPM.0000000000000219.
 37. Qaseem A, Wilt TJ, Weinberger SE, Hanania NA, Criner G, van der Molen T, et al. Diagnosis and management of stable chronic obstructive pulmonary disease: a clinical practice guideline update from the American College of Physicians, American College of Chest Physicians, American Thoracic Society, and European Respiratory Society. *Ann Intern Med*. 2011;155(3):179–191; doi: 10.7326/0003-4819-155-3-201108020-00008.
 38. Ries AL, Bauldoff GS, Carlin BW, Casaburi R, Emery CF, Mahler DA, et al. Pulmonary rehabilitation: Joint ACCP/AACVPR Evidence-Based Clinical Practice Guidelines. *Chest*. 2007;131(5 Suppl):4S–42S; doi: 10.1378/chest.06-2418.
 39. The Management of Chronic Obstructive Pulmonary Disease Working Group. VA/DoD clinical practice guideline for the management of chronic obstructive pulmonary disease. Washington: Department of Veterans Affairs, Department of Defense; 2014. Available from: <https://www.healthquality.va.gov/guidelines/CD/copd/VA-DoDCOPDCPG2014.pdf>.
 40. Marciniuk DD, Brooks D, Butcher S, Debigare R, Dechman G, Ford G, et al. Optimizing pulmonary rehabilitation in chronic obstructive pulmonary disease – practical issues: a Canadian Thoracic Society Clinical Practice Guideline. *Can Respir J*. 2010;17(4):159–168; doi: 10.1155/2010/425975.
 41. Bemard S, Ribeiro F, Maitais F, Saey D. Prescribing exercise training in pulmonary rehabilitation: a clinical experience. *Rev Port Pneumol*. 2014;20(2):92–100; doi: 10.1016/j.rppneu.2013.10.005.
 42. Bisca GW, Camiilo CA, Cavaiheri V, Pitta F, Osadnik CR. Peripheral muscle training in patients with chronic obstructive pulmonary disease: novel approaches and recent advances. *Expert Rev Respir Med*. 2017;11(5):413–423; doi: 10.1080/17476348.2017.1317598.
 43. Lacasse Y, Brosseau L, Miine S, Martin S, Wong E, Guyatt GH, et al. Pulmonary rehabilitation for chronic obstructive pulmonary disease. *Cochrane Database Syst Rev*. 2002;3:CD003793; doi: 10.1002/14651858.CD003793.