Review Article

Respiratory Rehabilitation and Chronic Obstructive Pulmonary Disease: An Exploratory Review

Mohammadreza Hajiesmaeili ¹, Seyed Hossein Ardehali ², Seyed Mohamadmasoud Moosavinasab ³, Mehdi Gharemani³, Sevak Hatamian ⁴, Sadegh Shabab ⁵, Amir Vahedian-Azimi ^{5*}

Abstract

Chronic obstructive pulmonary disease (COPD) is one of the few major causes of death whose prevalence is continuing to rise in the world. Pulmonary rehabilitation (PR), as a component of the treatment protocol, should be considered for all patients with chronic respiratory disease who have persistent symptoms. The purpose of the study was to investigate PR in patients with COPD, following six questions including comprehensive definition, nature's mechanism, commencing indication, advantages and disadvantages, comprehensive dimensions, and the cornerstone dimension of PR. The University of York Center for Reviewers and Dissemination Guidance approach was used for searching seven databases (Science Direct, Ovid, Cochrane, Ebsco Host, Scopus, Pub Med, and SID) with nineteen keywords and different combinations of aforesaid nineteen keywords from the year 1985 to the January 2015. Thirty full texts met the inclusion criteria and were analyzed for responding to the six research questions. The results showed that PR consists of exercise training, education, nutritional intervention, support in self-management behaviors, and psychosocial support. The extensive review of the literature indicated exercise training is the cornerstone of PR, but the study also corroborated that psychological aspect of the patients with COPD is the most important and the first dimension in PR. Furthermore, before the commencing any education, the patients with COPD in any stages, must have an effective and useful psychological support for ameliorating and improving the applicability of the PR.

Keywords: Pulmonary rehabilitation, Chronic Obstructive Pulmonary Disease, Exploratory Review

- Clinical Research Development Center of Loghman Hakim Hospital, Shahid Beheshti University of medical Sciences, Tehran, Iran
 Shohada Tajrish Hospital, Shahid Beheshti
- University of Medical Sciences, Tehran, Iran 3. Anesthesiology Research Center, Shahid
- Beheshti University of Medical Sciences, Tehran, Iran
- 4. Alborz University of Medical Sciences, Karaj, Iran
- 5. Trauma Research Center, Nursing Faculty, Baqiyatallah University of Medical Sciences, Tehran, Iran

* Corresponding Author

Vahedian-azimi A.

Trauma Research Center, Nursing Faculty, Baqiyatallah University of Medical Sciences, Tehran, Iran

E-mail: Amirvahedian@bmsu.ac.ir

Received: 2015/03/13 Revised: 2015/05/27 Accepted: 2015/06/19

1. Introduction

Chronic Obstructive Pulmonary Disease (COPD) is, a progressive disorder that often leads to respiratory failure, the most common cause of respiratory failure (1, 2). COPD is a growing public health problem both in developed and developing countries (3), is one of the few major causes of death whose prevalence is continuously rising in the world (4) which can occur on exertion or, in some individuals, at rest (5). It is currently the fourth leading cause of death in the world, and it is the only one of the top-ten chronic diseases still with a rising mortality in patients with COPD (3). These patients exert great strain on health care budgets and are frequent consumers of health care resources (6). From forty percent to fifty percent of patients with COPD discharged from hospitals are readmitted during the subsequent year and also seventeen percent of patients discharged from emergency departments require hospitalization (3, 4). The major cause

of hospitalization in COPD patients is acute exacerbation and, despite optimal pharmacologic therapy, these patients often have symptoms that limit normal physical activities and impair their quality of life (3, 4, 6). In this regard, Pulmonary rehabilitation (PR), as a component of the treatment protocol, should be considered for all patients with chronic respiratory disease who have persistent symptoms, have limited activity, or are unable to adjust to illness despite optimal medical management (3). PR has become an established part of the management of COPD and partially restores function (7). However, the implementation of PR remains a challenge, and one potential reason is the limited availability of studies concluding an improvement in health care resources (3). The in-depth experiences of the researchers demonstrated that from several parts of PR, psychological support is the most important components of PR; although it is opposite with other related researches (8-13). Furthermore, the

International Journal of Medical Reviews, Volume 2, Issue 2, Spring 2015; 230-237

Ş

purpose of the study was to investigate PR in the patients with COPD. The study questions were:

- 1. What is the comprehensive definition of PR?
- 2. What is the mechanism of PR?
- 3. What is the commencing indication of PR?
- 4. What are the advantages and disadvantages of PR?
- 5. What are the comprehensive dimensions of PR?
- 6. What is the cornerstone dimension of the PR?

2. Methods

For conducting the exploratory review study, the University of York Center for Reviewers and Dissemination Guidance approach was used as research framework (14, 15). This approach has seven steps. The steps are included as the following:

First step: Research question formulation

The research questions of the study were six questions including 1. What is the comprehensive definition of PR? 2. What is PR nature's mechanism? 3. What is the commencing indication of PR? 4. What are the advantages and disadvantages of PR? 5. What are the comprehensive dimensions of PR? and 6. What is the cornerstone dimension of the PR? The purpose of the exploratory review study was to investigate PR in the patients with COPD that conducted from the year 1985 to the 2015.

Second step: Defining search strategy

An extensive breadth of the available and existing databases were used including Science Direct, Ovid, Cochrane, Ebsco, Scopus, Pub Med, and Scientific Information Database (SID) with searching keywords such as "rehabilitation", "rehabilitation aspects", rehabilitation "rehabilitation program", "rehabilitation therapy", medical", "chronic disease of respiratory system", "chronic respiratory system disease", pulmonary rehabilitation", "lung rehabilitation", "rehabilitation lung", "rehabilitation "pulmonary rehabilitation", pulmonary", "respiratory rehabilitation", "chronic respiratory disease", "chronic respiratory failure", "chronic obstructive pulmonary disease", "chronic obstructive lung disease", "COPD", "COLD", and different combinations of aforesaid words. For finding more related articles, the references of the searched articles were comprehensively investigated. Keywords in the selected databases utilized in title, abstract and keywords domains. It should be noted that some databases have overlapping from citing article views and some articles are cited in several databases. Reference manager software (Endnote version 7) was used to prevent re-entry of retrieved articles.

Third step: Setting the inclusion and exclusion criteria

The inclusion criteria for including the article were: literature from 1985 to January 2015; literature in English and Persian languages; having electronic published research articles in formal peer-reviewed scientific journals; congruency between topics and the study questions and purpose; application of the different aspects of PR in patients with COPD; and originality of the paper. According to the third step, 33854 articles were found including 677 articles in Science Direct, 30927 articles in Ovid, 76 articles in Cochrane, 659 articles in Ebsco host, 15 articles in Scopus, 1424 articles in Pub Med, and 76 articles in SID. Based on the inclusion criteria, 195 English articles were retained.

Fourth step: Designing quality investigation checklist

A checklist was designed according to the inclusion criteria and the articles were assessed accordingly.

Fifth step: Usage of the checklist

The articles were investigated according to the full text. After quality checks of the articles, only 30 articles were retained.

Sixth step: Deriving the question's responses

Based on the six questions, the responses were extracted from the retained articles in the review process.

Seventh step: Combination of the derived information

Combination of the derived information in the point of the study questions and purpose were done in this step. Figure 1 demonstrates the flow diagram of article selection.



Figure 1. Flow Diagram of article selection

3. Results

From 33854 articles in the first step, the only 30 articles remained in the last step. The core concepts in PR scope were related to the definition, mechanism, benefits and non-benefits effects, commencing indications, PR dimensions and related discussion about the PR dimensions. In the following, the question's responses explained, respectively.

First question: Comprehensive definition of PR

Several definitions are cited in the related articles, but the comprehensive definition had two parts that are "evidence-based, multidisciplinary and comprehensive intervention for patients with chronic respiratory disease who are symptomatic and often have decreased daily life activities" (16-18) and "PR integrated into the individualized treatment of the patient". Its goals are to reduce symptoms including breathlessness, optimize functional status, improve participation in everyday activities (19) and reduce healthcare costs through stabilizing or reversing systemic manifestations of the disease (10, 11).

Second question: PR nature's mechanism

There is an interesting fact for the rationale of PR. The fact is, PR has virtually no direct effect on pulmonary physiology or function. It does indirectly reduce dynamic hyperinflation in COPD by reducing ventilatory requirements for exercise, thereby permitting breathing at a slower rate and allowing the patient to exhale more completely. Despite the non-effect on lung function, PR does lead to substantial improvement in dyspnea, exercise performance, functional status, healthcare utilization, and health-related quality of life (13, 20). In fact, the positive signal in these areas often substantially exceeds that of pharmacologic therapy. This apparent paradox is explained by the fact that much of the morbidity of COPD stems from its systemic effects (13).

Third question: The commencing indications

According to the American Thoracic Society/European Respiratory Society (ATS/ERS) standards for the Diagnosis and Management of the Patients with COPD and the Global Initiative for Obstructive Lung Disease (GOLD) Guidelines, commencement of PR can be considered with disease of moderate severity (21-23). The classification of the GOLD Criteria is presented in table 1 (24).

Fourth question: Advantages and disadvantages of PR

Although effects of PR have been recognized in patient groups, responses of individual patients to this intervention are highly variable (7, 13). PR has been shown to be effective in improving health status and exercise capacity in patients with COPD (25). Associated co-morbidities of COPD that may be reversible with therapy including PR are reduced activity levels, physical de-conditioning following the adoption of a sedentary lifestyle, peripheral muscle defects in oxidative enzymes, muscle fiber, reductions in peripheral muscle mass, improper pacing during exercise, fear of dyspnea-producing activities, low self-confidence in walking ability, poor coping skills, and lacking collaborative disease management skills (13, 19, 24, 26-28).

Regarding to the disadvantages, the extensive review of the literature explains that PR has no disadvantages and

non-benefits effects. Despite the fact that PR is an effective option for those with moderate or severe disease, it may not be indicated for the specific patient, geographically available, desired by the patient, or covered by the insurance company (13).

Fifth question: Comprehensive dimensions of PR

The domains of PR are so wide and extensive because PR includes the rehabilitation of not only patients with respiratory failure in need of ventilatory support but also patients with primary pulmonary disease. PR consists of exercise training, education, nutritional intervention, support in self-management behaviors, and psychosocial support. The domains are explained fully in the Discussion section.

Sixth question: The cornerstone dimension of PR

The researches' experiences indicated that the psychological aspects and dimensions of PR are the cornerstone and most important part of the PR program. Furthermore, before commencing any education, patients with COPD in any stages must have an effective and useful psychological support for ameliorating and improving the applicability of the PR.

4. Discussion

The purpose of the study was to investigate the PR concept in the patients with COPD with six questions including comprehensive PR definition, nature's mechanism, commencing indication, advantages and disadvantages, comprehensive dimensions and finally the cornerstone dimension of PR. It should be noted that clinician must then administer the therapies on an asneeded basis. These therapies range from smoking cessation, promotion of a healthy lifestyle, promoting activity in the home setting, teaching self-management strategies (especially early recognition and treatment of the COPD exacerbation), recommending exercise, optimizing bronchodilator and other pharmacologic therapies, addressing nutritional depletion, and recognizing and providing psychosocial support. Furthermore, although the patients with COPD have several therapies as described above, PR is higher concept and can be summarized in different ways. Those completing PR have shown measurable improvement in quality of life, symptoms, exercise performance, depression and anxiety, and health care utilization (10, 27). Other researches explained that PR often leads to significant and clinically meaningful improvements in outcome areas of importance to the patient including relief of dyspnea, improvement in exercise performance, and enhancement of functional status and quality of life. These results have been demonstrated in controlled trials (29, 30) and substantiated by meta-analyses (17, 18, 31)., It can be concluded that the

proven benefits of PR include increased exercise capacity, reduced dyspnea, improved health-related quality of life, and decreased healthcare utilization (13). For the importance of the issue, the domains of PR are concisely explained in the following.

4.1. Education and Collaborative Self-Management Strategies

Education, which permeates all aspects of PR, should be tailored to the needs of the individual. Important aspects of education include promotion of a healthy lifestyle (including incorporating exercise and activity into daily life), early recognition and treatment of the COPD exacerbation, and the importance of long-term adherence to therapy. These elements are components of collaborative self-management, which is of considerable importance in the long-term management of COPD (13, 32-34) (Table 2).

There are evidence-based recommendations for the exercise component, including the intensity, frequency, and type of exercise necessary, but there is a limited research with which to direct the content and delivery of the education component. A lack of knowledge about COPD was consistent across all patients, who were generally dissatisfied with the amount of information they were given when diagnosed as having COPD and during their continuing care. They were unclear about the etiology of COPD. The results of the extensive review of the literature explain that patients and health professionals were ambivalent about the amount of information given

about the trajectory and progression of COPD. The patients wanted information, but some felt that discussing issues such as living wills and end-of-life was inappropriate in a group setting. The health professionals also believed patients with COPD have a poor understanding of the disease and agreed that information about the disease and its progression should be given to patients during their rehabilitation. There was a consensus that information about end-of-life issues should be given on an individual basis and that a group format was inappropriate for that topic (16). Moreover, development of such a component has been highlighted as an important area for research. Considering the importance of the issue, Key education topics and suggested content, and key factors for the format and delivery of the educational component of PR for patients with COPD are presented in Table 3 (16).

4.2. Exercise Training

Although the researches' experiences of the study indicate the psychological aspects and dimensions of the PR is the cornerstone and most important of the PR program, the review of the literature indicated exercise training is the cornerstone of PR (8, 10-13). The literature explained that the PR improves exercise tolerance in patients with COPD independent of a direct effect on lung function. This reflects its positive effects on the structural, biochemical, and physiologic abnormalities in the peripheral muscles of patients with COPD (8-11).

Table 1. Global Initiative for Obstructive Lung Disease Criteria (24)		
Level of COPD	Criteria	Treatment
Mild (stage 1)	FEV1 / FVC <70% predicted FEV1 ≥80% predicted With or without symptoms	1. Short-acting bronchodilator
Moderate (stage 2)	FEV1 / FVC <70% predicted FEV1 between 50% and 80% predicted With or without symptoms	 Regular treatment with 1 or more bronchodilators; Rehabilitation Inhaled glucocorticosteroids if significant symptoms and improved FEV1
Moderate (stage 3)	FEV1 / FVC <70% predicted FEV1 between 30% and 50% predicted With or without symptoms	 Regular treatment with 1 or more bronchodilators; Rehabilitation Inhaled glucocorticosteroids if significant symptoms and improved FEV1 or if repeated exacerbations
Severe (stage 4)	FEV1 / FVC <70% predicted FEV1 <30% predicted Or presence of respiratory failure or right heart failure	 Regular treatment with 1 or more bronchodilators; Rehabilitation Inhaled glucocorticosteroids if significant symptoms and improved FEV1, or if repeated exacerbations Treatment of complications (osteoporosis, diabetes, hypertension, pulmonary hypertension) Long-term oxygen therapy (LTOT) Consider surgical options such as transplantation or lung- volume reduction surgery

Table 2. Key education topics and suggested content for PR in COPD population (16)			
Key Education Topics	Suggested Content		
Disease education: "When you are first diagnosed they say 'Oh yes, you've got COPD,' but that's the end of it, nobody tells you or explains anything to you" (<i>PR group, male, moderate disease</i>).	Anatomy and pathophysiology of COPD, causes, disease progression		
Management of breathlessness and the physical impact of COPD: " I can't walk from the living room to the toilet when I am having a bad day" (<i>PR group, female, moderate</i> <i>disease</i>).	Practical strategies for ADLs, walking, pacing, panic reduction, energy conservation, positions of ease, benefits of exercise, work simplification		
Management of an exacerbation: "I'm inclined to hold on and say, 'No. This is a cold and I'm going to get better" (<i>PR</i> <i>group, female, severe disease</i>).	Recognition of worsening symptoms, when and where to seek help, feedback about management decisions		
Medication: "Nobody tells you how to take it [inhaler] or when to take it"(<i>PR group, male, moderate disease</i>).	How, when, and why to use medications. Potential medication interactions, contraindications, and regime feasibility. Cross-infection and equipment maintenance		
Psychosocial support:_ "Depression is the biggest problem. It is the worst, because if you were an active person all your life and now you're inactive, it's hard to accept" (<i>Non-PR group, male, mild disease</i>).	Management of psychosocial symptoms, including management of depression, panic, anger, and frustration. Information about, and benefit of, support groups. Making lifestyle adjustments (such as, role reversal)		
Welfare and benefits system: "I am horrified to hear that people are not getting their allowances There are so many things out there to help us but many of us don't know about them" (<i>PR group, female, severe disease</i>).	Information on and benefit of support groups. Welfare and benefits system disability entitlements, access to home aids and appliances		
Table 3. Key Factors for the Format and Delivery of the Educational Component of Pulmonary Rehabilitation (16)			
Suggested Format	Suggested Delivery		
Format and method of delivery: "If other people have the same thing, I would like to know how they cope with it; it might help me" (<i>PR group, male, moderate disease</i>).	Group format with peer support, practical demonstrations, visual aids and models, consider education prior to exercise session. Offer a range of formats, including video, DVD, leaflet, website.		
Educator and delivery method: "I think the doctors would be talking in talk we wouldn't understand, using these words that would mean nothing to us" (<i>Mixed group, female, severe disease</i>).	Credible and knowledgeable individual, layman's language.		
Location: "I think it [pulmonary rehabilitation] should be hospital-based because I think you are coming into an environment that is very health conscious, you know, it is for our benefit. If you went to a town hall or the gym you wouldn't	Convenient, accessible, local, access for disabled, adequate parking for cars.		

disease). **Duration and frequency:** "It would take you to get the first one over [first education session] and then you would say that's been good, I could do with another few [education] sessions" (*Mixed group, male, severe disease*).

Supplementary information: "You should have a leaflet made for the disease with diagrams on the side. If you are short of breath, what to do. Then as the stages go on and you know you are going to get worse in later years. You know the symptoms that you are looking for" (*PR group, female, moderate disease*).

have the same confidence" (PR group, female, moderate

Long-term support: "I think if you went to the exercises outside the clinic with people who haven't got what you got, I think it would make me feel I'm ill" (*PR group, female, moderate disease*).

Provide supplemental information to support delivery of the educational topics during PR.

Provide additional information on topics not covered (including end of life/living wills, airway clearance, sexual relationships and intimacy, oxygen therapy, and others).

Arrange follow-up and provide appropriate opportunities for ongoing exercise and social support

Exercise reconditioning can improve the ability to perform specific tasks and is the cornerstone of PR (12); furthermore, the advantages of the exercise training in patients with COPD can be summarized as several points including: 1. A minimum of 20 sessions should be given $\geq 3 \times$ per week to achieve physiologic benefits (two supervised sessions per week plus one unsupervised home session may also be acceptable); 2. High-intensity exercise produces greater physiologic benefit and should be encouraged (low-intensity training is effective for those who cannot achieve this level); 3. Interval training may be useful in promoting higher levels of exercise training in more symptomatic patients; 4. Both upper and lower extremity training should be used; 5. The combination of strength and endurance training has multiple beneficial effects and is well tolerated; and 6. Strength training is particularly indicated for patients with significant muscle atrophy or weakness (13). In this regard, an American College of Chest Physicians and American Association of Cardiovascular and Pulmonary Rehabilitation consensus group recently reported that patients with COPD who undergo a program of lower extremity exercise training consistently improve parameters of exercise tolerance. Several studies have also reported significantly greater improvements in endurance for COPD patients by highintensity rather than low-intensity exercise (12).

4.3. Psychosocial Intervention

Nearly forty-five percent of patients with moderate to severe COPD have depressive symptoms (35). Patients asserted that COPD had a considerable psychosocial impact on their lives (36). They consistently reported experiencing depression and frustration associated with their chronic illness, and they also described panic, anger, social isolation, and a loss in confidence that had affected their ADLs (13, 16). Additionally, anxiety over dyspnea producing activities may promote a maladaptive sedentary lifestyle. Patients appeared to have previously had stereotypically gender roles within their households and found it difficult to adjust to role reversal because of COPD. Female patients reported having difficulty doing housework and described how their partners had to learn how to cook; similarly, male patients described difficulties with gardening, household maintenance, and washing their cars (29). Also, the lack of access to a clinical psychologist was a barrier to providing expert psychosocial support for patients. Additionally, the health professionals agreed that information about intimate relationships is important but that the topic is not suitable for group discussion (16). Furthermore, developing an adequate social support system, learning stress reduction techniques including muscle relaxation, imagery, yoga, and addressing specific problems including sexual intimacy, partner/spousal

dependency are addressed in PR (10, 11). Established on the mentioned matters, the first step for applicability of the PR program in patients with COPD is availability of the psychological support and cohesive and consistent related program to patients have enough preparedness for effective participation in the other programs. In other words, the first step of the patients with COPD is providing effective psychological and psychiatric consultation and support that be along with effective and comprehensive educations in different aspects of the patient's needs. It may be concluded the psychological and psychiatric consultation and support along with PR can be easier and faster than other times and professional team members can run the programs in higher level for the patients.

4.4. Nutritional Intervention

About a third of patients with moderate to severe COPD also suffer from involuntary weight loss and muscle wasting. Underweight patients with COPD have a worse prognosis, independent of other severity markers for COPD (11). Treatment of nutritional depletion and body composition abnormalities requires interventions in the form of caloric, physiologic, and/or pharmacologic therapy (13). Nowadays, pulmonary therapy is applied beside others because combining PR with other forms of COPD therapy may enhance the overall outcome (13). For instance, higher intensity training and bronchodilator therapy are complementary and also optimization of bronchodilator therapy enhances the effectiveness of PR and exercise training adds to the gains from bronchodilator therapy (37). Oxygen therapy is another supplementary therapy for patients with COPD due to Oxygen supplementation -even for patients with COPD without significant exercise-induced hypoxemiaand also enhances outcomes from exercise training (38, 39).

5. Conclusion

PR includes of exercise training, education, nutritional intervention, support in self-management behaviors, and psychosocial support. Although a large amount of the literature indicates the cornerstone and most important component of the PR is exercise training, in-depth researchers' experiences from working with patients with COPD demonstrated that the cornerstone and most important component of PR is psychological support. From one side it is a prelude to effective education and from other side has a significant role for applicability of given and provided education. Furthermore, as an overall, and as a result's extract of the study, psychological support in the patients with COPD is the first dimension of the PR and in the other dimensions of the PR, the

education, support in self-management behaviors and nutritional intervention are placed, respectively.

Acknowledgment

We thank to Clinical Research Development Center of Loghman Hakim Hospital, Shahid Beheshti University of Medical Sciences, Tehran, Iran for their methodological and financial support. And also, we thank Kirk Allen from AuthorAid for assisting with editing the English of the article.

References

- 1. Decramer M. Response of the respiratory muscles to rehabilitation in COPD. Journal of applied physiology (Bethesda, Md : 1985). 2009;107(3):971-6.
- 2. Decramer M. Treatment of chronic respiratory failure: lung volume reduction surgery versus rehabilitation. The European respiratory journal Supplement. 2003;47:47s-56s.
- Rubí M, Renom F, Ramis F, Medinas M, Centeno MJ, Górriz M, et al. Effectiveness of Pulmonary Rehabilitation in Reducing Health Resources Use in Chronic Obstructive Pulmonary Disease. Archives of Physical Medicine and Rehabilitation. 2010;91(3):364-8.
- Rizzi M, Grassi M, Pecis M, Andreoli A, Taurino AE, Sergi M, et al. A Specific Home Care Program Improves the Survival of Patients With Chronic Obstructive Pulmonary Disease Receiving Long Term Oxygen Therapy. Archives of Physical Medicine and Rehabilitation. 2009;90(3):395-401.
- 5. Lord VM, Cave P, Hume VJ, Flude EJ, Evans A, Kelly JL, et al. Singing teaching as a therapy for chronic respiratory disease--a randomised controlled trial and qualitative evaluation. BMC pulmonary medicine. 2010;10:41.
- 6. Putt MT, Watson M, Seale H, Paratz JD. Muscle Stretching Technique Increases Vital Capacity and Range of Motion in Patients With Chronic Obstructive Pulmonary Disease. Archives of Physical Medicine and Rehabilitation. 2008;89(6):1103-7.
- Trappenburg JC, Troosters T, Spruit MA, Vandebrouck N, Decramer M, Gosselink R. Psychosocial Conditions Do Not Affect Short-Term Outcome of Multidisciplinary Rehabilitation in Chronic Obstructive Pulmonary Disease. Archives of Physical Medicine and Rehabilitation. 2005;86(9):1788-92.
- Maltais F, LeBlanc P, Simard C, Jobin J, Bérubé C, Bruneau J, et al. Skeletal muscle adaptation to endurance training in patients with chronic obstructive pulmonary disease. American journal of respiratory and critical care medicine. 1996;154(2):442-7.
- Maltais F, LeBlanc P, Whittom F, Simard C, Marquis K, Bélanger M, et al. Oxidative enzyme activities of the vastus lateralis muscle and the functional status in patients with COPD. Thorax. 2000;55(10):848-53.
- Nici L, Donner C, Wouters E, Zuwallack R, Ambrosino N, Bourbeau J, et al. American thoracic society/European respiratory society statement on pulmonary rehabilitation. American journal of respiratory and critical care medicine. 2006;173(12):1390-413.
- 11. Nici L, Zuwallack R. Scope, background and definition of pulmonary rehabilitation. European journal of physical & rehabilitation medicine. 2011;47(3):465-74.
- 12. Gimenez M, Servera E, Vergara P, Bach JR, Polu J-M. Endurance training in patients with chronic obstructive pulmonary disease: A comparison of high versus moderate

intensity. Archives of Physical Medicine and Rehabilitation. 2000;81(1):102-9.

- 13. ZuWallack R, Hedges H. Primary Care of the Patient with Chronic Obstructive Pulmonary Disease—Part 3: Pulmonary Rehabilitation and Comprehensive Care for the Patient with Chronic Obstructive Pulmonary Disease. The American Journal of Medicine. 2008;121(7, Supplement 1):S25-S32.
- Vahedian-Azimi A, Ebadi A, Saadat S, Ahmadi F. What is an Appropriate Nursing Care Model in Critical Care Units: Domestic or International Models. International Journal of Medical Reviews. 2014;1(2).
- 15. Higgins JP, Green S. Cochrane handbook for systematic reviews of interventions: Wiley Online Library; 2008.
- Wilson JS, O'Neill B, Reilly J, MacMahon J, Bradley JM. Education in Pulmonary Rehabilitation: The Patient's Perspective. Archives of Physical Medicine and Rehabilitation. 2007;88(12):1704-9.
- Lacasse Y, Martin S, Lasserson T, Goldstein R. Metaanalysis of respiratory rehabilitation in chronic obstructive pulmonary disease. A Cochrane systematic review. Europa medicophysica. 2007;43(4):475-85.
- Lacasse Y, Wong E, Guyatt GH, King D, Cook DJ, Goldstein RS. Meta-analysis of respiratory rehabilitation in chronic obstructive pulmonary disease. The Lancet. 1996;348(9035):1115-9.
- 19. Liddell F, Webber J. Pulmonary rehabilitation for chronic obstructive pulmonary disease: a pilot study evaluating a once-weekly versus twice-weekly supervised programme. Physiotherapy. 2010;96(1):68-74.
- ZuWallack R, Hashim A, McCuskerl C, Nonnandin E, Benoit-Connors M, Lahiri B. The trajectory of change over multiple outcome areas during comprehensive outpatient pulmonary rehabilitation. Chronic respiratory disease. 2006;3(1):11-8.
- 21. Celli BR. Pulmonary Rehabilitation For Patients With Advanced Lung Disease. Clinics in Chest Medicine. 1997; 18(3):521-34.
- 22. Celli BR. Chronic respiratory failure after lung resection: the role of pulmonary rehabilitation. Thoracic Surgery Clinics. 2004;14(3):417-28.
- Gómez FP, Rodriguez-Roisin R. Global Initiative for Chronic Obstructive Lung Disease (GOLD) guidelines for chronic obstructive pulmonary disease. Current opinion in pulmonary medicine. 2002;8(2):81-6.
- Alba AS, Kim H, Whiteson JH, Bartels MN. Cardiopulmonary Rehabilitation and Cancer Rehabilitation.
 Pulmonary Rehabilitation Review. Archives of Physical Medicine and Rehabilitation. 2006;87(3, Supplement):57-64.
- 25. O'Neill B, McKevitt A, Rafferty S, Bradley JM, Johnston D, Bradbury I, et al. A Comparison of Twice- Versus Once-Weekly Supervision During Pulmonary Rehabilitation in Chronic Obstructive Pulmonary Disease. Archives of Physical Medicine and Rehabilitation. 2007;88(2):167-72.
- 26. Berton DC, Silveira L, Da Costa CC, De Souza RM, Winter CD, Zimermann Teixeira PJ. Effectiveness of Pulmonary Rehabilitation in Exercise Capacity and Quality of Life in Chronic Obstructive Pulmonary Disease Patients With and Without Global Fat-Free Mass Depletion. Archives of Physical Medicine and Rehabilitation. 2013;94(8):1607-14.
- 27. Motegi T, Yamada K, Ishii T, Gemma A, Kida K. Long-term management of chronic obstructive pulmonary disease: A survey of collaboration among physicians involved in pulmonary rehabilitation in Japan. Respiratory Investigation. 2012;50(3):98-103.
- 28. Carrai R, Scano G, Gigliotti F, Romagnoli I, Lanini B, Coli C, et al. Prevalence of limb muscle dysfunction in patients with chronic obstructive pulmonary disease admitted to a

pulmonary rehabilitation centre. Clinical Neurophysiology. 2012;123(11):2306-11.

- 29. Ries AL, Kaplan RM, Limberg TM, Prewitt LM. Effects of pulmonary rehabilitation on physiologic and psychosocial outcomes in patients with chronic obstructive pulmonary disease. Annals of internal medicine. 1995;122(11):823-32.
- 30. Griffiths T, Burr M, Campbell I, Lewis-Jenkins V, Mullins J, Shiels K, et al. Results at 1 year of outpatient multidisciplinary pulmonary rehabilitation: a randomised controlled trial. The Lancet. 2000;355(9201):362-8.
- Lacasse Y, Goldstein R, Lasserson T, Martin S. Pulmonary rehabilitation for chronic obstructive pulmonary disease. Cochrane Database Syst Rev. 2006;4(4).
- 32. Puhan MA, Behnke M, Devereaux PJ, Montori VM, Braendli O, Frey M, et al. Measurement of agreement on health-related quality of life changes in response to respiratory rehabilitation by patients and physicians—A prospective study. Respiratory Medicine. 2004;98(12):1195-202.
- 33. Puhan MA, Chandra D, Mosenifar Z, Ries A, Make B, Hansel NN, et al. The minimal important difference of exercise tests in severe COPD. The European respiratory journal. 2011 Apr;37(4):784-90.
- 34. 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.

- 35. Mills TL. Comorbid depressive symptomatology: isolating the effects of chronic medical conditions on self-reported depressive symptoms among community-dwelling older adults. Social Science & Medicine. 2001;53(5):569-78.
- 36. Barr RG, Celli BR, Martinez FJ, Ries AL, Rennard SI, Reilly JJ, et al. Physician and patient perceptions in COPD: the COPD resource network needs assessment survey. The American journal of medicine. 2005;118(12):1415. e9-. e17.
- 37. Casaburi R, Kukafka D, Cooper CB, Witek TJ, Kesten S. Improvement in exercise tolerance with the combination of tiotropium and pulmonary rehabilitation in patients with COPD. Chest Journal. 2005;127(3):809-17.
- Emtner M, Porszasz J, Burns M, Somfay A, Casaburi R. Benefits of supplemental oxygen in exercise training in nonhypoxemic chronic obstructive pulmonary disease patients. American journal of respiratory and critical care medicine. 2003;168(9):1034-42.
- 39. Somfay A, Porszasz J, Lee S, Casaburi R. Dose-response effect of oxygen on hyperinflation and exercise endurance in nonhypoxaemic COPD patients. European Respiratory Journal. 2001;18(1):77-84.