BALNEO RESEARCH JOURNAL
English Edition
eISSN 2069-7619 pISSN 2069-7597 ROMANIAN ASSOCIATION OF BALNEOLOGY

Music, A "Body-Mind Medicine" In Rehabilitation Programs of Patients with Chronic Obstructive Pulmonary Disease

MAIEREAN Anca Diana[1], TONCA Claudia[2], PERNE Mirela Georgiana[3*], DOGARU Gabriela[4], RAJNOVEANU Ruxandra[1], CHIS Ana Florica[1], MOTOC Nicoleta Stefania[1], BORDEA Roxana Ioana[5]

Corresponding author: **PERNE Mirela-Georgiana**, E-mail: albmirela@yahoo.ro

Balneo Research Journal DOI: http://dx.doi.org/10.12680/balneo.2020.375 Vol.11, No.4, December 2020 p: 431–443

[1] "Iuliu Hatieganu" University of Medicine and Pharmacy, Cluj-Napoca, Romania
[2] Clinical Hospital of Pneumology "Leon Daniello" Cluj-Napoca, Romania
[3] "Iuliu Haţieganu" University of Medicine and Pharmacy, Cluj-Napoca, Romania
[4] "Iuliu Haţieganu" University of Medicine and Pharmacy, Cluj-Napoca, Romania
[5] "Iuliu Hatieganu" University of Medicine and Pharmacy, Cluj-Napoca, Romania

Abstract

Chronic obstructive pulmonary disease (COPD) is a progressive disease characterized by dyspnea and chronic cough. The main risk factor is cigarette smoking, but there are other ones implicated in the COPD etiology such as air pollution, childhood asthma, aging, chemical exposure, dietary factors, and genetic predisposition. Besides, COPD is associated with several comorbidities that influence prognostic and management, like asthma, lung cancer, obstructive sleep apnea, cardiovascular disease, metabolic syndrome, and depression or anxiety. The management is multidisciplinary and its role is to ease symptoms, prevent complications, slow disease progression, and improve the quality of life. In the last years, many alternative techniques have been implemented such as speleotherapy, halotherapy, muscular training, neuromuscular electrostimulation, acupuncture, thermotherapy, and music therapy. From those, music therapy has become a form of "mind-body medicine" indispensable in rehabilitation programs, whether used actively or passively, and has gained a lot of interest in alternative medicine.

Keywords: *COPD, music therapy, alternative medicine,*

Introduction

Chronic obstructive pulmonary disease (COPD) is a common and preventable disease characterized by shortness of breath and chronic cough due to airways narrowing over time. If not treated properly, this condition evolves, has a worse prognostic and becomes difficult to reverse. The main cause of COPD is cigarette smoking but other factors can increase the risk, such as airway pollution, genetics and asbestos exposure. Spirometry is required to confirm the diagnosis of COPD, by calculating the ratio of the forced expiratory volume in the first second (FEV1) and the forced vital capacity (FVC) (1-3).

In the last years, COPD has become an important public health challenge that affects the daily living and the quality of life of patients. This is the reason why a multidisciplinary approach that includes an integrative intervention is required. The management of COPD patients should follow three steps: smoking cessation, reduction of acute exacerbation and comorbidity management. Besides these three cornerstones, the clinicians should take into consideration other alternative therapies, such as speleotherapy, halotherapy, muscle training, soft tissue manual therapy intervention, neuromuscular electrostimulation and music therapy, to improve outcomes for patients with COPD (4-6).

The development of alternative therapies has become a solution to multiple health concerns and in the last years, it has been integrated into various treatment plans. Recently, music therapy gained a role as an addition to the treatment of the chronic condition (7).

Prevalence

COPD has a rise in prevalence in the last decades is more common in ex-smokers and higher smokers compared to non-smokers and in men compared to women, reaching in 2020 a global prevalence of 11.8% in men and 8.5% in women. Also, the aging of the population increases the prevalence of COPD, in those over 40 years old compared to those under 40 years (2). Globally, there are 3 million deaths annually and the World Health Organization (WHO) predicts that COPD will become the third leading cause of death worldwide in 2030 (2,8).

This disease represents a serious economic burden, with direct healthcare costs due to the higher number of exacerbation-related hospitalizations and indirect costs because of loss of home productivity (8,9).

Pathophysiology

Cigarette smoking represents the primary cause of COPD worldwide but many other risk factors have been identified, such as atmospheric pollution, passive smoking, excessive exposure to fumes (mainly charcoal used for domestic cooking and wood) and other inhaled gases and noxious particles (10-12).

The lung abnormalities characteristic of COPD is produced by the inhalation of these products that cause a chronic inflammatory response and oxidative stress.

Moreover, after the inhalation of the offending agent ends, other pathobiological processes are included in the progression of the disease, like genetically determined responses, accelerated lung aging, alteration of the microbiome, inappropriate control of programmed cell death, imbalance of proteinases and anti-proteinases, an abnormal interaction between environment and microbiome, abnormal ion transport and pulmonary endothelial cell dysfunction (11,13).

Together, all these mechanisms can cause pathological modifications in the individual's lung compartments: lung parenchyma, pulmonary vasculature, peripheral airways and central airways. These changes lead to the specific characteristics of COPD which include excessive mucus secretion, ciliary dysfunction, emphysema, airflow limitation, abnormal gas exchange, pulmonary hypertension, hyperinflation and numerous systemic effects (11).

Etiology

Cigarette smoking is the main factor involved in the development of COPD by increasing the lung and systemic inflammation, systemic oxidative stress and by affecting the endothelial and vasomotor function, predisposing to a pro-coagulant state. Habitual smoking does not influence only the airways, but also other systems, increasing the incidence of comorbidities in patients with COPD: skeletal muscle abnormalities, diabetes, ischemic heart disease, hypertension, heart failure and cancer (14,15).

However, smoking is not the only risk factor for COPD and many studies published in the last years documented COPD cases in individuals that never smoked. Therefore, there are other factors involved in the COPD etiology, such as air pollution, indoor pollution (biomass), childhood asthma, chemical exposure, aging, dietary factors and genetic predisposition (16,17).

Air pollution integrates the particulate matter (which includes acids, metals, soil or dust particles and organic chemicals), nitrogen dioxide and ozone, responsible for alveolar damage, changes in the chemical composition of lung lavage fluids and lung inflammation (12,18).

Comorbidities

Comorbidities are defined as being coexisting diseases or conditions that influence COPD severity, diagnosis or management and lead to multiple exacerbations and increased hospitalization risk. They are also associated with poor adherence to therapeutic interventions, higher mortality and reduced quality of life (19).

COPD is frequently associated with multiple comorbidities, the most common being asthma, bronchiectasis, lung cancer, cardiovascular diseases (CVDs), osteoporosis, skeletal muscle dysfunction, metabolic disorders (including obesity), depression and anxiety (14).

Asthma

Because COPD is a pathology that affects the small airways and causes a parenchymal injury, it is often a challenge to establish the differential diagnosis between COPD and asthma. Even if the symptomatology is very similar, an accurate diagnosis is important to establish the optimum treatment plan (19). Despite this, in a subset of subjects, older than 40 years old, which associate an airflow limitation and have a history of asthma or high bronchodilator reversibility, the clinicians could establish the diagnosis of asthma-COPD overlap syndrome (ACO). ACO affects about a quarter of patients with COPD and almost a third of patients who previously had asthma and it is characterized by an increased risk of hospital admissions due to exacerbations, worse respiratory symptomatology and poorer quality of life. The management of ACO is very complex including therapy that targets neutrophilic, eosinophilic or paucigranulocytic airway inflammation and also specific interventions of respiratory rehabilitation (19,20).

Lung cancer

Large epidemiological studies revealed a high prevalence of lung cancer in COPD subjects moreover because both pathologies showed common risk factors, such as smoking and increasing age. Besides, the presence of the neoplasm is associated with the severity of airway obstruction, so subjects with severe stages of COPD have an important prevalence of lung cancer. At the time of histological diagnosis, COPD patients have a poorer prognostic with a 3-year survival rate of 15%, significantly lower than in patients without COPD, so smoking cessation and other rehabilitation techniques have gained a central role in the management plan. However, non-smoker subjects diagnosed with lung cancer, that associate emphysema or chronic bronchitis are at a higher risk of mortality (6,21,22).

Obstructive sleep apnea (OSA)

The overlap syndrome is represented by the association between COPD and obstructive sleep apnea (OSA) and has a prevalence between 1% and 3.6% in the general population, being responsible for hypoventilation episodes during sleep with nocturnal desaturation, poor sleep quality, increased nocturnal hypoxemia, daytime hypercapnia and a higher rate of mortality. In COPD patients, a low body mass index is protective against the development of OSA. Contrary, subjects with a high grade of the upper airway and systemic inflammation have a greater risk for OSA, an association that plays an additive or synergistic role in the development of cardiovascular comorbidities (22-24). In COPD patients with impaired gas exchange and diagnosed with pulmonary hypertension not explained by lung function, OSA should be suspected and treated when typical nocturnal symptoms such as poor sleep, snoring or witnessed apnea and daytime signs such as excessive

daytime sleepiness, headache and morning fatigue are present (22,25).

Cardiovascular Diseases

Vascular and heart diseases developed due to endothelial dysfunction and coagulopathy are among the most important comorbidities observed in COPD with a direct impact on patient survival and quality of life, being responsible for a greater depletion of health resources (22).The most common cardiovascular pathologies diagnosed in COPD patients are coronary heart disease, cardiac arrhythmias, arterial hypertension and heart failure (2).

Coronary heart disease and essential hypertension are pathologies often diagnosed in patients with COPD, due to the presence of systemic inflammatory response and C-reactive protein (CRP) elevation. A study that evaluated 897 COPD patients showed that in 27.6% of patients were found sequelae of myocardial infarction and also 30% of subjects had a known history of myocardial infarction, with a negative impact on survival (22,26,27).

Cardiac arrhythmias also represent a common disease associated with COPD and there is a bidirectional relationship between the acute exacerbation of COPD and the development of atrial fibrillation (AF), mostly because AF is often associated with lower FEV1. The presence of AF does not influence the COPD treatment, but in this case, the patient needs short-acting beta2-agonists and caution is advised because the administration of these drugs may trigger AF, which becomes harder to control (28,29).

Heart failure and COPD. COPD and heart failure are pathologies that show the same risk factors like smoking and often the same symptomatology, the reason why both pathologies remain frequently underdiagnosed. Both have similar pathophysiological mechanisms like systemic inflammation, skeletal muscle dysfunction and pump failure. Also, both diseases have to be taken into consideration in the elderly patients presenting for dyspnea, moreover because their clinical presentation can be very similar (22,30).

Metabolic syndrome

The metabolic syndrome is a challenge in COPD subjects and includes high blood glucose levels and/ or insulin resistance, central obesity, atherogenic dyslipidemia, elevated triglycerides and higher blood pressure. The pro-inflammatory and the pro-thrombotic state are responsible for the increase of acute-phase reactants, fibrinogen and plasminogen activator inhibitors causing a higher grade of systemic inflammation. In addition, both COPD and metabolic syndrome have similar risk factors such as smoking and some common pathophysiological mechanisms. Between these comorbidities there is a complex relation, so type 2 diabetes subjects often associate hypertension, cardiovascular diseases and obesity. COPD patients with diabetes and obesity have a reduced lung function, higher levels of CRP (C-reactive protein), IL-6 (Interleukin-6) and TNF-α (Tumor Necrosis Factor-α) compared to non-COPD patients, modifications known to be risk factors for major cardiovascular events (14,31,32). In recent years, in literature, a COPD patient paradox was described, showing that patients with higher body mass index (BMI) had longer survival. This paradox is no longer valid in patients with higher carbon dioxide levels and impaired exercise capacity, mostly because these two modifications impact the survival rate (33).

Depression and anxiety

Depression is considered a mental state characterized by pessimism, lassitude and reduced self-esteem. In COPD patients, clinical depression is found in about 40% of cases, but the pathology is more common in subjects that do not meet diagnostic criteria and in the elderly (22,34). On the other hand, anxiety is diagnosed in patients with indefinable insecurity and its prevalence among people with COPD is about 10% - 30% (22).

Both anxiety and depression have a synergistic role and are associated with lower self-efficacy of symptom management and consecutively with a poor health-related quality of life. It was stipulated that there is a higher rate of treatment failure and mortality in patients with acute exacerbation of COPD if they were diagnosed previously with depression or anxiety and also a greater risk of readmission in the following 30 days (35-37). Regvat et al. demonstrated that patients with anxiety and/or depression perceived dyspnea more often and intensely, the reason why in their medical history the first hospitalization for COPD occurs sooner (38). In addition, in patients with anxiety or panic disorder, it was proven that the airway obstruction is more important, the reason why specific questionnaires, careful monitoring and pulmonary rehabilitation with an integrated approach show significant improvement (39).

Diagnostic

The diagnosis of COPD should be taken into consideration in individuals with a history of exposure to risk factors such as cigarette smoke, occupational or environmental pollutants and/or a positive family history of obstructive lung diseases which present in pulmonology medical services with symptoms like dyspnea, chronic cough or sputum production lasting more than usually. Many subjects, especially women and young people underestimate their symptoms and limit their physical activity in order to minimize them, the reason why the diagnostic of COPD is delayed (40).

The clinicians must perform spirometry tests that measure the forced expiratory volume in first second (FEV1), and the forced vital capacity (FVC) and to calculate the ratio between these values (Tiffeneau Index

– TI = FEV1/FVC) which should reach a value under 0.7 for a positive diagnosis (7,41).
In the last years, a new strategy has been developed to provide a more comprehensive assessment of COPD patients that includes a combination of a score of symptoms, risk of exacerbations, degree of airflow limitation and presence of comorbidities in order to do not overestimate its presence in older people or underestimate its presence in younger ones (41).

Management

The COPD management is multidisciplinary and its role is to prevent complications, ease symptoms, generally slow disease progression and improve the quality of life. COPD is a debilitating disease with symptoms that affect the quality of life of patients, being responsible for higher rates of morbidity and mortality. Therefore it is important to develop new treatment techniques that can improve the symptomatology and impact the rates of hospital admission, the activities of daily living and the severity of exacerbations (5).
In the last years, a lot of alternative techniques have been successfully implemented in COPD patients management, like speleotherapy, halotherapy, muscular training, neuromuscular electrostimulation, acupuncture, thermotherapy and music therapy (4,5).
In the treatment of COPD, speleotherapy involves using normal salt in a reserved atmosphere. It was described a unique microclimate seen in karst caves that can offer a lack of pollutants, a constant air temperature, moderate to high humidity and fine aerosols elements (magnesium, sodium, calcium, potassium). This alternative therapy improves respiratory function, oxygen saturation, the partial pressure of oxygen and carbon dioxide in arterial blood in COPD patients (42,43). In addition, it showed improvements in six minute walking distance and also in the clinical state of stable COPD patients, meaning a decreasing of symptomatology, a reduction of exacerbation and hospital admission and an improvement of physical tolerance and fatigue (43,44). Moreover, other studies showed that rehabilitation programs that included speleotherapy had positive results on depression and anxiety of COPD patients (4).
Halotherapy is a method used as an alternative for speleotherapy and consists in the inhalation of small salt particles in a controlled environment that replicate the microclimate of a salt cave. Halotherapy has many effects, like the improvement of immunity, bactericidal effect and improvement in proprieties of airway secretion, being associated with a relief of respiratory symptoms. It was proved that halotherapy has a beneficial effect on lung volumes, six-minute walking distance and quality of life (43,45,46).
It is a well-known fact that COPD patients develop dynamic hyperinflation due to changes in the anatomy of the airways and lung parenchyma, modification responsible for an increase of end expiratory lung volume that limits tidal volume and respiratory capacity. For these reasons, respiratory muscle training is important in stable COPD patients since it has benefits on pulmonary function and respiratory muscle strength. Inspiratory muscle training can reduce the dyspnea, improve the functional capacity, the quality of life and the six-minute walking distance (47-49). In obese COPD patients the association between caloric restriction and resistance exercise training showed an improvement on symptoms, health status and functional capacity. In addition, recent studies proved that respiratory muscle weakness is a risk factor for frequent exacerbations that lead to hospitalizations, so expiratory muscle training should be introduced in order to increase exercise performance (50-52).
In COPD patients a peripheral muscle dysfunction characterized by weakness, atrophy, metabolic and structural changes of the limb muscles has a negative impact on exercise capacity. Several studies reported various benefits of pulmonary rehabilitation including neuromuscular electrostimulation (NMES) in six-minute walking distance, exercise tolerance due to the increasing of endurance and strength of lower limbs skeletal muscles (53,54).
Acupuncture therapy has been widely used in the treatment of a variety of chronic conditions. In people with COPD, acupuncture may reduce bronchial inflammation and promote the release of immunomodulatory and vascular factors (55). Jungfei et al. showed, in a multicenter study that included 72 subjects, that acupuncture is associated with a decrease of the Borg scale after six-minute walking test and with an increased six-minute walking distance. In addition, the same study stipulated that there was an increase in the lowest oxygen saturation measured while performing six-minute walking test and also the subjects had an improvement in health-related quality of life (56).
Thermotherapy includes thermal and mineral bath therapy, near infrared hyperthermia treatment and hydroelectric bath therapy. Lin et al observed a positive effect of thermotherapy and balneotherapy in COPD patients with an improvement in pulmonary function and quality of life (57).
Taking into account that COPD patients associate a high proportion of physical comorbidities such as cerebrovascular disease, obesity, muscle abnormalities and arthrosis that limit their ability to participate in common exercise training, McNamara et al. proposed water-based exercise training. This method showed improvement in endurance, dyspnea, six-minute walking distance and fatigue (58).

Music Therapy

Music therapy is a form of "body-mind medicine" conducted along with rehabilitation programs in order to bring a clinical change. There are two ways for clinicians to use music, as active or passive therapy, in the management of chronic respiratory conditions. Active mode involves subjects singing or playing a musical instrument while passive therapy involves listening to various type of music. Previous studies showed that live music provided by a music therapist is more efficient than recorded music (59,60).

Active music therapy

Singing is a complex activity which involves the use of the lungs for air supply in order to create large lung volumes. In this procedure, exhalation becomes an active process which requires good posture and active diaphragm contraction (61). Singing implies rhythmical, strong and fast inhalations followed by active and regulated exhalations which demands focused control of breathing in order to reduce hyperventilation and alter irregular breathing. In addition, music therapy can involve some respiratory techniques such as Pursed Lips Breathing or Blowing against resistance that may reduce hyperinflation, modify the respiratory pattern, enhance diaphragmatic movement and reinforce respiratory muscles (62,63). Pursed lips breathing is represented by a nasal inhalation followed by a slow expiratory blowing against partially closed lips. This technique is used when playing wind instruments like harmonica, recorder, melodica, to asses a diaphragmatic breathing, body posture and to achieve expiratory airways pressure (7).

Singing increases the use of vital capacity up to 90% in order to increase the tidal volume, modification that can minimize atelectasis, helping to clear secretions through airway oscillations and increase the force of cough reflex (63). Bonilha et al. observed that after singing classes, in COPD patients, there was an improvement in both maximal inspiratory and expiratory pressure, a decrease in expiratory reserve volume, a transitory elevation in dyspnea, with no statistically significant differences on pulmonary function. However, routine singing in subjects with dyspnea cause desensitization of breathlessness by improving the breathing coordination and by reducing the anxiety associated with respiratory symptoms (64).

Moreover, Engen et al. observed a change of the clavicular breathing pattern to a diaphragmatic one in just one week of singing intervention (65). COPD subjects which participated in therapeutic singing activities noted positive effects on wellbeing, an improvement in quality of life, amelioration of depression and a better mood (66-68). Holland et al. assessed the role of music therapy in COPD and found no improvements in exercise capacity, appreciated by six-minute walking test, even if short programs of singing may ameliorate single breath counting and possibly maximum expiratory capacity (69). Contrary, McNaughton et al. conducted a study in COPD patients which had completed a program of pulmonary rehabilitation and were included in singing groups for one year. They observed a significant increase of six-minute walking distance in the singing group and also an increased sense of social connection which may explain the reduction of the anxiety (70). In another study, Lord et al. noticed a reduction of anxiety symptoms and also an improvement of physical component score of the Saint George health related quality of life short form questionnaire (SGRQ) (71).

Ho et al. proved that COPD subjects that follow a home exercise plan accompanied by music achieved the desired exercise intensity (72). In addition, Thaut et al. observed that by adding rhythmic auditory stimulation to increase the rhythm of the music, the patients with stroke had an increased walking speed, step cadence, velocity and stride length (73). Moreover, music is responsible for affecting a person's mood, decreasing perceived breathlessness and improving the walking distance (74). Another study that used music with different speeds during an upper extremity training program observed a decrease of the dyspnea sensation in COPD subjects. Still, it is difficult to determine the effects of certain types of music on the outcomes, because many subjects included in various studies selected their favorite music while exercising in order to achieve a pleasant environment to keep them motivated (72).

Brooks et al. concluded that in some COPD subjects, moderate tempo music prevents the level of breathlessness from getting worse after a 10 minutes walk, even if the music did not affect anxiety or tolerance for physical activity (75). Contrary, Thornbi et al. reported lower levels of perceived dyspnea, an increase of 22% of the six-minute walking distance and with 53% more steps while listening to music (76). Reychler et al. studied the effects of listening to ambient music during pulmonary rehabilitation session and showed that there was no influence on the perceived exertion, dyspnea, fatigue or cardiorespiratory parameters, but a decrease of anxiety symptoms (77).

Moreover, listening to music during high intensity exercise had a positive effect on COPD symptoms, by reducing the dyspnea and increasing the endurance time (78). Some data from literature highlighted the effect of wind instrument playing on the respiratory system. Results showed higher lung function values in wind musicians and a higher prevalence of mild respiratory infection than in the control group (7). Alexander et al. examined the role of a harmonica playing in COPD subjects during the rehabilitation program and found that they had improvements in the quality of life, shortness of breath and walking distance (79). Moreover, Hart. et al observed that after a 12-week harmonica program for two hours a week, the patients had an increase in maximum

expiratory pressure and in six-minute walking distance (80).

Passive music therapy

Listening to music is associated with numerous mental and physical benefits for people who are diagnosed with COPD including relaxation, improved mood, reduced perceived exertion and improved exercise capacity. Because of its ability to affect emotional changes, listening to music may be a powerful tool in the rehabilitation program of COPD patients. Quick paced music is generally invigorating and it facilitates movement and expression, while slower paced music has a calming effect, reducing anxiety levels and it physiologically correlates with a decrease of blood pressure (81). In a study conducted by Lee et al. dyspnea was significantly reduced, with more than 1 point in the Borg dyspnea scale, during exercise training while listening to music. Another study showed that there was a notable increase in endurance time with 1:10 minutes when listening to music compared to the group that did not benefit from that. Also, a reduction in dyspnea was reported in those who listened self-selected music, including individual preference in artist and style, compared to those who listened investigator-selected music. In contrast, music had no effect on oxygen saturation, leg fatigue and heart rate (82).

Dance

Physical activity is one of the most important and effective components of pulmonary rehabilitation programs in patients with pulmonary chronic diseases. Despite its benefits, completion rates are poor and access is variable. However, there are other forms of physical activity that should be taken into consideration, such as dance. Some studies in COPD subjects included dance sessions, both community and during hospital admission and their preliminary results proved that it can improve a range of health outcomes (83,84).

Moreover, dance and music were included in a pulmonary rehabilitation program and showed improvements in interest and enthusiasm, with a reduction of anxiety and depression, both in participants and staff delivering the programs (81).

Conclusion

COPD is a leading cause of morbidity, mortality, and resource use worldwide. Although pharmaceuticals have been extensively studied and utilized, their disease-modifying effects are limited and dependent on patient adherence.

Pulmonary Rehabilitation has emerged over the last decade as an essential component to an integrated approach in the management of COPD. The treatment of this disease has expanded to include a variety of rehabilitative practices, including music therapy. Music therapy applied both in active or passive way is a promising and effective method to reduce anxiety, depression, perceived dyspnea, enhance sense of control and increase the quality of life of patients suffering from COPD.

References:

1. WHO. The World Health Report 2002. Available at:http://www.who.int/whr/2002/en/, Apr 8 2013. Accessed online at 20th June 2020.
2. Global Strategy for the Diagnosis, Management and Prevention of Chronic Obstructive Pulmonary Disease, Global Initiative for Chronic Obstructive Lung Disease (GOLD), 2020 Report.
3. Budin CE, Marginean C, Bordea IR, Enache LS, Enache EL, Grigorescu BL, et al. The influence of smoking on nicotine exposure biomarkers and inflammatory profile among Foster care teenagers. Chimia. 2018;69(12):3659-63.
4. Alexescu TG, Maierean AD, Ciumarnean L, Budin C, Dogaru G, et al. Rehabilitation therapies in stable chronic obstructive pulmonary disease. Balneo Research Journal. 2019;10(1):37-44.
5. Criner G, Dreher M, D'Ambrosio CM, Zuwallack R, Geiseler J, Pepin JL. COPD Advanced patient management. Chest Journal. 2018;153(6):1497-8.
6. Vremaroiu-Coman A, Alexescu TG, Negrean V, Milaciu MV, Buzoianu AD, Ciumarnean L, Todea AD. Ethical aspects of smoking cessation among the population from Transilvania. Balneo Research Journal. 2018;9(3):254-9.
7. Panigrahi A, Sohani S, Amadi C, Joshi A. Role of music in the management of chronic obstructive pulmonary disease (COPD): A literature review. Technology and Healthcare. 2013;22(2014):53-61.
8. Welte T, Vogelmeier C, Papi A. COPD: early diagnosis and treatment to slow disease progression. Int J Clin Pract.2015;69(3):336-49.
9. Anzueto A. Impact of exacerbations on COPD. Eur Respir Rev. 2010;19: 113–8.
10. Yohannes AM, Junkes-Cunha M, Smith J, Vestbo J. Management of Dyspnea and Anxiety in Chronic Obstructive Pulmonary Disease: A Critical Review. J Am Med Dir Assoc. 2017;18(12):e1-e17.
11. Celli BR, Decramer M, Wedzicha JA, et al. An Official American Thoracic Society/European Respiratory Society Statement: Research questions in chronic obstructive pulmonary disease. Am J Respir Crit Care Med. 2015;191(7):e4-e27.
12. Todea DA, Suatean I, Coman AC, Rosca LE. The effect of climate change and air pollution on

allergenic potential of pollens. Notulae Botanicae Horti Agrobotanici. 2013;41(2):646-50.
13. Repine JE, Bast A, Lankhorst I; Oxidative Stress Study Group.Oxidative stress in chronic obstructive pulmonary disease. Am J Respir Crit Care Med 1997;156:341–57.
14. Fabbri LM, Luppi F, Beghe B, Rabe KF. Complex chronic comorbidities of COPD. Eur Respir J.2008;31:204-12.
15. Budin CE, Alexescu TG, Bordea IR, Gherginescu MC, Aluas M, et al. Nicotine addiction objective in educational programs for smoking prevention in young people. Chimia. 2019;70(6):2168-72
16. Salvi SS, Barnes PJ. Chronic obstructive pulmonary disease in non-smokers. Lancet 2009; 374: 733–43.
17. Postma DS, Bush A, van den Berge M. Risk factors and early origins of chronic obstructive pulmonary disease. Lancet. 2015;385(9971):899-909.
18. Hansel NN, McCormack MC, Kim V. The Effects of Air Pollution and Temperature on COPD. COPD. 2016;13(3):372-9.
19. Maierean A, Ciumarnean L, Alexescu TG, Domokos B, Ranjnoveanu R, et al. Complementary therapeutic approaches in asthma. Balneo Research Journal. 2019;10(3):204-12.
20. Leung JM, Sin DD. Asthma-COPD overlap syndrome: pathogenesis, clinical features, and therapeutic targets. BMJ. 2017;358:j3772.
21. Todea D, Cosma C, Dicu T, Rosca L, Cucos (Dinu) A, et al. Lung cancer risk induced by residential radon in Cluj and Alba counties, Romania. Environmental Engineering and Management Journal.2013;12(6):1281-5.
22. Cavaillès A, Brinchault-Rabin G, Dixmier A, et al. Comorbidities of COPD. Eur Respir Rev. 2013;22(130):454-75.
23. Maierean A, Perne MG, Tonca C, Man M, Dantes E, et al. Adherence to CPAP therapy - a necessity in the pulmonary rehabilitation of patients with Obstructive sleep apnea. Balneo Research Journal. 2020;11(2):210-219.
24. Todea D, Herescu A, Rosca L. Obstructive sleep apnea syndrome – a matter of public health. Transylvanian Review of Administrative Sciences. 2012;37E:186-201
25. Budin CE, Ciumarnean L, Maierean A, Ranjnoveanu R, Gergely BD, et al. Therapeutic alternavies with CPAP in obstructive sleep apnea. J Mind Med Sci. 2019;6(2):181-89.
26. Falk JA, Kadiev S, Criner GJ, Scharf SM, Minai OA, Diaz P. Cardiac disease in chronic obstructive pulmonary disease. Proc Am Thorac Soc. 2008 May 1;5(4):543-8.
27. Alexescu TG, Bordea IR, Cozma A, Rajnoveanu R, Buzoianu AD, et al. Metabolic Profile and the Risk of Early Atheroschlerosis in Patients with Obesity and Overweight. Rev Chim. 2019;70(10):3627-33.
28. Onishi K. Total management of chronic obstructive pulmonary disease (COPD) as an independent risk factor for cardiovascular disease. J Cardiol. 2017;70(2):128-34.
29. Alexescu TG, Tarmure S, Negrean V, Cosnarovici M, Ruta MV, et al. Nanoparticles in the Treatment of Chronic Lung Diseases. Journal of Mind and Medical Sciences. 2019;6(2):224-31.
30. Guder G, Störk S. COPD and heart failure: differential diagnosis and comorbidity. Herz. 2019;44(6):502-08.
31. Zalar DM, Pop C, Buzdugan E, Todea D, Mogosan CI. The atherosclerosis- inflammation relationship – a pathophysiological approach. Farmacia. 2019;67(6):941-7.
32. Milaciu MV, Ciumărnean L, Sampelean D, Negrean V, Milaciu C, Acalovschi M. Non-cardiometabolic comorbidities of non-alcoholic fatty liver disease. Balneo Res J. 2018; 9(2): 43-49.
33. James BD, Jones AV, Trethewey RE, Evans RA. Obesity and metabolic syndrome in COPD: Is exercise the answer? Chron Respir Dis. 2018;15(2):173-81.
34. Aydin IO, Ulusahin A. Depression, anxiety comorbidity, and disability in tuberculosis and chronic obstructive pulmonary disease patients: applicability of GHQ-12. Gen Hosp Psychiatry. 2001;23:77–83.
35. Dahlen I, Janson C. Anxiety and depression are related to the outcome of emergency treatment in patients with obstructive pulmonary disease. Chest 2002;122:1633–7.
36. Crockett AJ, Cranston JM, Moss JR, Alpers JH. The impact of anxiety, depression and living alone in chronic obstructive pulmonary disease. Qual Life Res 2002;11:309–16.
37. Ng TP, Niti M, Wan-Cheng T, et al. Depressive symptoms and chronic obstructive pulmonary disease. Arch Intern Med 2007; 167: 60–67.
38. Regvat J, Zmitek A, Vegnuti M, et al. Anxiety and depression during hospital treatment of exacerbation of chronic obstructive pulmonary disease. J Int Med Res 2011; 39: 1028–38.
39. Spitzer C, Gla¨ser S, Grabe HJ, et al. Mental health problems, obstructive lung disease and lung

function: findings from the general population. J Psychosom Res 2011; 71: 174–79.
40. Barnes PJ, Burney PG, Silverman EK, et al. Chronic obstructive pulmonary disease. Nat Rev Dis Primers. 2015;1:15076.
41. Lange P, Halpin DM, O'Donnell DE, MacNee W. Diagnosis, assessment, and phenotyping of COPD: beyond FEV_1. Int J Chron Obstruct Pulmon Dis. 2016; 11(Spec Iss): 3–12.
42. Kendrová L, Takáč P, Kubincová, Mikuľáková W, Nechvátal P. Effect of spa treatment and speleotherapy in the treatment of chronic obstructive pulmonary disease – a pilot study. CSWHI 2016;7(2):7–15.
43. Rashleigh R, Sheree MS, Roberts NJ. A review of halotherapy for chronic obstructive pulmonary disease. International Journal of COPD 2014:9 239–24.
44. Zajac J, Bojar I, Helbin J, Kolarzyk E, Owoc A. Salt caves as simulation of natural environment and significance of halotherapy. AAEM. 2014;21(1):124-7.
45. Nurov I. Immunologic features of speleotherapy in patients with chronic obstructive pulmonary disease. Medical and Health Science Journal. 2010;2:44–47.
46. Wise RA, Brown CD. Minimal clinically important differences in the six-minute walk test and the incremental shuttle walking test. COPD. 2005 Mar;2(1):125-9.
47. Montecinos CC, Godoy-Olave D, Contreras-Briceno FA, Gutierrez P, Torres-Castro R, et al. The immediate effect of soft tissue manual therapy intervention on lung function in severe chronic obstructive pulmonary disease. International Journal of COPD 2017; 12; 691-6.
48. Neves LF, Reis MH, Plentz RDM, Matte DL, Coronel CC, Sbruzzi G. Expiratory and Expiratory Plus Inspiratory Muscle Training Improves Respiratory Muscle Strength in Patients with COPD: Sustematic Review. Respiratory Care 2014 April; 59(9):1-9.
49. Beaumont M, Forget P, Couturaud F, Reychler G. Effects of inspiratory muscle training in COPD patients: A systematic review and meta-analysis. Clin Respir J. 2018 April; 12;2178-88.
50. Mcdonald VM, Gibson PG, Scott PG, Baines PJ, Hensley MJ, et al. Should we treat obesity in COPD? The effects of diet and resistance exercise training. Respirology. 2016; 21:875-882.
51. Vilaro´ J, Ramirez-Sarmiento A, Martínez-Llorens JM, Mendoza T, Alvarez M, Sa´nchez-Cayado N, et al. Global muscle dysfunction as a risk factor of readmission to hospital due to COPD exacerbations. Respir Med .2010;104(12):1896-1902.
52. Illi SK, Held U, Frank I, Spengler CM. Effect of respiratory muscle training on exercise performance in healthy individuals: a systematic review and meta-analysis. Sports Med. 2012;42(8):707-724.
53. Kucio C, Niesporek J, Kucio E, Narloch D, Węgrzyn B. Evaluation of the Effects of Neuromuscular Electrical Stimulation of The Lower Limbs Combined with Pulmonary Rehabilitation on Exercise Tolerance in Patients with Chronic Obstructive Pulmonary Disease. Journal of Human Kinetics volume. 2016 Dec;54:75-82.
54. Hill K, Cavalheri V, Mathur S, Roig M, Janaudis-Ferreira T, Robles P, Dolmage TE, Goldstein R. Neuromuscular electrostimulation for adults with chronic obstructive pulmonary disease. Cochrane Database Syst Rev. 2018 May 29;5:CD010821
55. Coyle ME, Shergis JL, Huang ET, et al. Acupuncture therapies for chronic obstructive pulmonary disease: a systematic review of randomized, controlled trials. Altern Ther Health Med 2014; 20:10–23.
56. Junfei F, Xuehui W, Xing L, Dejun Z, Jinquan X. Acupuncture for Chronic Obstructive Pulmonary Disease (COPD): a multicenter, randomized, sham-controled trial. Medicine (Baltimore). 2016;95(40):e4879
57. Lin FL. Effects of balneotherapy on pulmonary function and quality of life in Chronic Obstructive Pulmonary Disease Patients. 2014 Published online. Available at https://sigma.nursingrepository.org/handle/10755/335348?show=full&fbclid=IwAR0H8HqmWtPWw8yIIbRsOsxpj7M4FzKgWQwMm5AIuWHKZbwISMSnxP-KFuM
58. McNamara R, McKeough Z, McKenzie DC, Alison JA. Water-based exercise in COPD with physical comorbidities: a randomized control trial. European Respiratory Journal. 2013;41(6):1284-91.
59. Kenny DT, Faunce G. The impact of group singing on mood, coping, and perceived pain in chronic pain patients attending a multidisciplinary pain clinic. J Music Ther 2004; 41: 241-58.
60. Eley R, Gorman D. Didgeridoo playing and singing to support asthma management in Aboriginal Australians. J RuralHealth 2010; 26: 100-4.
61. McNamara RJ, Epsley C, Coren E, McKeough ZJ. Singing for adults with chronic obstructive pulmonary disease (COPD). Cochrane Database Syst Rev. 2017;12(12):CD012296

62. Canga B, Azoulay R, Raskin J, Loewy J. AIR: Advances in Respiration - Music therapy in the treatment of chronic pulmonary disease. Respir Med. 2015;109(12):1532-9.
63. Goodridge D, Nicol JJ, Horvey KJ, Butcher S. Therapeutic singing as an adjunct for pulmonary rehabilitation participants with COPD: Outcomes of a feasibility study. Music and Medicine. 2013;5(3):169–76.
64. Bonilha AG, Onofre F, Vieira ML, Prado MY, Martinez JA.Effect of singing classes on pulmonary function and quality of life of COPD patients. Int J Chron Obstruct Pulm Dis.2009;4:1-8.
65. Engen R. The singer's breath: implications for treatment of persons with emphysema. J Music Ther.2005;42(1):20-48
66. Clift S, Nicol JJ, Raisbeck M, Whitmore C, Morrison I. Group singing, wellbeing and health: a systematic mapping of research evidence. UNESCO J. Multi-Disciplinary Res Arts. 2010;2(1):1-25.
67. Gick ML. Singing, health and well-being: a health psychologist's review. Psychomusicology. 2011;21(1-2):176-207.
68. Irons JY, Kenny DT, McElrea M, Chang AB. Singing therapy for young people with cystic fibrosis: a randomized controlled trial. Music Med. 2012;4(3):136-45
69. Holland AE, Hill CJ, Rasekaba T, Lee A, Naughton MT, McDonald CF. Updating the minimal important difference for six minute walk distance in patients with chronic obstructive pulmonary disease. Arch Phys Med Rehab. 2010;91(2):221-5.
70. McNaughton A, Weatherall M, Williams M, et al. Sing Your Lungs Out-a community singing group for chronic obstructive pulmonary disease: a 1-year pilot study. BMJ Open. 2017;7(1):e014151.
71. Lord VM, Cave P, Hume VJ, et al. Singing teaching as a therapy for chronic respiratory disease--a randomised controlled trial and qualitative evaluation. BMC Pulm Med. 2010;10:41.
72. Ho CF, Maa SH, Shyu YI, Lai YT, Hung TC, Chen HC. Effectiveness of paced walking to music at home for patients with COPD. COPD. 2012;9(5):447-47.
73. Th aut MH, Leins AK, Rice RR, Argstatter H, Kenyon GP, McIntosh GC, Bolay HV, Fetter M. Rhythmic auditory stimulation improves gait more than NDT/Bobath training in near-ambulatory patients early poststroke: a single-blind, randomized trial. Neurorehabil Neural Repair 2007 Sep-Oct; 21(5):455–9.
74. Bauldoff GS, Hoff man LA, Zullo TG, Sciurba FC. Exercise maintenance following pulmonary rehabilitation: eff ect of distractive stimuli. Chest 2002 Sep; 122(3):948–54.
75. Brooks D, Sidani S, Graydon J, McBride S, Hall L, Weinacht K. Evaluating the effects of music on dyspnea during exercise in individuals with chronic obstructive pulmonary disease: a pilot study. Rehabil Nurs. 2003;28(6):192-6.
76. Thornby MA, Haas F, Axen K.Effect of distractive auditory stimuli on exercise tolerance in patients with COPD. Chest.1995; 107:1213-7.
77. Reychler G, Mottart F, Boland M, et al. Influence of ambient music on perceived exertion during a pulmonary rehabilitation session: a randomized crossover study. Respir Care. 2015;60(5):711-7.
78. Dolmage TE, Rhim M, Goldstein RS, Brooks D. The Impact of Listening to Music During a High-Intensity Exercise Endurance Test in People With COPD. Chest. 2018;153(5):1134-41.
79. Alexander JL, Wagner CL. Is harmonica playing an effective adjunct therapy to pulmonary rehabilitation? Rehabil Nurs. 2012;37(4): 207–12.
80. Hart MK, Stewardson E, Jamil AK, Tecson KM, Millard MW. Usefulness of harmonica playing to improve outcomes in patients with chronic obstructive pulmonary disease. Proceedings (Baylor University. Medical Center). 2020;33(2):178–82.
81. Philip K, Lewis A, Hopkinson NS. Music and dance in chronic lung disease. Breathe.2019; 15: 116–20.
82. Lee AL, Dolmage TE, Rhim M, Goldstein RS, Brooks D. The Impact of Listening to Music During a High-Intensity Exercise Endurance Test in People With COPD. Chest. 2018;153(5):1134-41.
83. Farmer C. Dance Well Evaluation Report 2016–2019. London, Akademi, 2018. Available from: https://akademi.co.uk/wp-content/uploads/2018/11/DW-Evaluation-Report-2018-FINAL-web.pdf
84. Fong Yan A, Cobley S, Chan C, et al. The effectiveness of dance interventions on physical health outcomes compared to other forms of physical activity: a systematic review and meta-analysis. Sports Med. 2018; 48: 933–51.