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Molecular dynamics in COPD following diets and environmental stressor: Obesity leverage of health care utilize Omics

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Abstract

Chronic obstructive pulmonary disease (COPD) represented as inflammatory complication of chronic bronchitis which is characterized by oxidative stress driven phenotypic changes likely enlarged alveoli and increased mucus along with tightened smooth muscle which exaggerate pathological consequences such as breathing problems. The association between COPD and obesity as a metabolic disorder following a variety of environmental stressors include lifestyle change (e.g., diet and e-smoking or marijuana) and air pollution are less likely to be evaluated. People who are suffering with COPD developed extensive suffocation and difficulty breathing, which ultimately leads to fatal conditions in severe cases, for example lung cancer, heart attack, and stroke.

Previous studies showed metabolic disorder like obesity appeared as a risk determinant to COPD like breathing problem or deep vein thrombosis and its genetic modification resulted from abnormality of molecular dynamics turned out key trigger in case of immune alteration and inflammation following exposure of several environmental factors which could be linked with comorbidity in secondary chronic diseases pairing with other metabolic disorders (e.g., diabetes, heart disease, cancer or fatty liver disease). Lifestyle changes along with physical activities and management of the diet is worth to reduce COPD symptomatic firing. However, environmental factors like air pollution or particle matter owing to industrialization and urbanization include a variety of dust within indoor life, certain type of e-smoke also triggers the establishment of emphysema and enhances the progression of COPD aligned with molecular alteration in the lung tissue or interaction between different organs. Prediction and prevention skills as key tools of health management and evaluation in case of COPD remains unclear.

Integrative care includes clinic assessment (e.g., the body mass index, diets, and metabolic profile using survey following physician guidance) could be coupled cellular and topological interaction between obesity and COPD supplemented with advanced functional and genetic variation utilize human genomics study like single nucleotide polymorphism (SNP). To understand the impact of environmental risk better (e.g., air pollution or particle matter) on pathogenesis of disease or onset of the disease underlying the pulmonary system stratified lifestyle, age, metabolic disorders, diets, and medications, we envision exploring risks such as disease barrier and social determinants along with detection tools which may assess molecular dynamics and their alteration following stress might be associated with COPD in the pathogenesis. Environmental stressors (e.g., air pollution, particle matter, food addictive chemicals, and stress) as epigenetic modifiers could attribute to early phase of COPD onset and pathogenesis which reflect the molecular dynamics and redirection of networking pathways depending on gut immunity. Profiling of secondary metabolites is worth to explicate intervention of metabolism cascade owing to alter molecular sensitivity and connectivity. Utilized multi-dimensional omics such as metabolomics, genomics with exome sequencing, and epigenomics, prevention and prediction skills could visualize a new angle of disease diagnostic under the platform of integrative health care and surveillance supporting to patient's quality of life.

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1. Introduction

Chronic obstructive pulmonary disease or COPD is a distinctive group of respiratory disorders and public burden related disease of the lungs where the patients usually have conditions such as emphysema or chronic bronchitis or both simultaneously [1, 2]. Emphysema conditions inflame and narrow the bronchioles and areolas within the patient's lungs, which significantly interfere with the inhalation process and the amount of gaseous exchange within the lungs of the patient [32]. This drives the development of extensive suffocation and difficulty in breathing which ultimately leads to fatal conditions in severe cases [1]. Chronic bronchitis is linked with the narrowing of the bronchus tubes of the patient due to the accumulation of mucus, which ultimately leads to the disruption of the breathing process, causing the disruption of the respiratory process and the gaseous exchange method within the lungs [19]. Obesity is one of the leading health risks for the development of chronic obstructive pulmonary disease [13, 16, 17, 19]. As a result, it can be stated that diet consideration and monitoring the obesity rate should be an important part of the health campaigns that are promoted to disrupt the triggering of developing COPD [28]. Compelling evidence supports that the fundamental problem beyond obesity: diet, and its influence has been provided in the research, followed by a comprehensive understanding of diet and obesity and their influence on COPD [4, 8, 24]. Research driven nutrient reports about the pathogenesis of COPD demonstrated that incorrect diet and obesity along with a viable intervention has also been provided in the research [28].

Up to date, it can be highlighted that obesity and diet are the fundamental causes that lead to the development of chronic obstructive pulmonary disorders [22, 28]. Obesity was substantially greater among COPD patients compared to those without COPD in a study of 650,000 people conducted as part of the Canadian National Health Survey (24.6 % and 17.1 %, respectively, $P < 0.001$) [16]. Obesity is a critical condition that is associated with the proportion of the risk factor for the development of specific medical conditions, including diabetes, cardiac problems, and pulmonary diseases, along with the development of musculoskeletal disorders [12]. Lainscak et al. (2011) examined the relationship between BMI and mortality in COPD using a retrospective survey of patients hospitalized for acute exacerbation of COPD and discovered that the optimum BMI for the lowest risk of death was overweight (BMI of 25.09–26.56 kg/m²) [18, 20]. Moreover, improper intake of diet also proposed the development of obesity which in turn causes the development of chronic obstructive pulmonary disorders [11, 22]. In mal-nourished individuals with COPD, nutritional intervention improves muscular strength, pulmonary function, physical performance, and overall quality of life [5, 10]. Therefore, it becomes one of the fundamental strategies to implement interventions to disrupt the development of chronic obstructive pulmonary diseases based on the factors that promote the establishment of obesity and improper diet [12]. However, less analytical research is done over the specific interventions and lifestyle alterations that must be integrated to mitigate the problem associated with the influence of obesity and diet on chronic obstructive pulmonary diseases [37, 38]. The development of proper interventions and lifestyle changes would be extremely important to relieve the concern of the Global community [13].

This review aims to understand the potential impact of Diet and Obesity on COPD about health intervention between metabolic disorder and risk assessment. The intervention focused on molecular alteration, including metabolism dysfunction and inflammation, generic vulnerability, and lifestyle following exposure to various environmental stressors.

1.1. Potential risk as Environmental stressor: Diet and Obesity

It has been analyzed that obesity interferes with the normal functioning of the pulmonary system due to the storage of excess fat in the thoracic region, which ultimately promotes the development of severe chronic obstructive pulmonary diseases [21]. The Global increase of the total number of the population who has COPD due to the development of obesity is increasing with time, and it is becoming a global concern [21]. In terms of the World Health Organization (WHO) reports, it was stated that in the year 2008, about 1.4 billion adults 35% of the world population considered to be significantly overweight, and about 200 million adults obese in accordance with their BMI values [11]. A population-based survey revealed a higher risk associated with the development of Chronic Obstructive Pulmonary Disease in individuals who have obesity and have prevented themselves in implementing a proper healthy diet structure [13]. A systematic survey has revealed an average increase in the overall population who have become susceptible to the development of obesity, which has increased the total number of patients having chronic obstructive pulmonary diseases (COPD) [16]. It has been reported that poor diet causes about 250 million deaths worldwide, which is often associated with two distinct diseases, including cardiovascular diseases and pulmonary diseases [14]. According to a critical analysis of the World Health Organization, about 44.4% of the pulmonary diseases of patients are associated with the overweight and obesity of patients due to improper diet intake [1]. There is an obstruction which reflects

malfunction of inflammatory signaling, adipokine signaling and alteration of muscle mass in those patients who are suffering lung complications due to accumulation of excess fat which may worsen the development of pulmonary diseases or lung disease. It suggests smoker with COPD in obese patients compare to lean decrease of FEV1 in the study [38]. However, there are still debate connectivity and interaction between inflammatory cytokines and adipokines. Along with the development of obesity as a driving factor for the establishment of COPD diseases, diet plays a crucial role and the risk factor for the development of distinctive chronic diseases including COPD by restructuring of microbiome profile in the gut and promoting molecular networking between gut and lung [33].

1.2. Pathogenesis of COPD in Obese Patients

The development of obesity due to poor health choices diminishes the functioning of the lungs and obstructs the arterial layer in the lungs of the patient due to the proportion of extensive pressure on the chest area of the patient [25]. This ultimately leads to the construction of the muscles of the lungs and thoracic region and results in the poor functioning of the respiratory system [25, 26]. Eventually the patient's offers from suffocation due to the poor gaseous exchange in the lungs of the patient and due to the inability of the patient to take in the expected amount of respiratory volume for maintaining proper respiratory process [18, 32] which leads to the development of chronic pulmonary obstructive diseases [27, 29, 36]. Moreover, there is a predominance of the secretion of lymphocytes, neutrophils, and macrophages on the ruptured areas of the skin of the lungs due to the accumulation of excess fat in the bronchial tubes and the air sacs of the lungs [6]. This leads to the development of infection, which is fundamentally characterized by the inflammation of the peripheral sex of the lungs and development of oxidative stress, which eventually leads to the development of emphysema and chronic bronchitis. Furthermore, the loss of the alveoli layer due to the infection caused due to fat accumulation in the lungs and the area in the thorax also leads to the development of apoptosis and protease imbalance which are also critical diseases under the major group of COPD [30, 35].

2. Intervention

The fundamental intervention that must be promoted to reduce the fatality associated with the development of COPD which is the increase in the level of the total number of the population who are obese and improper lifestyle choices, including an imbalance in the diet system [1]. Implementation of proper analysis of the population through the provision of screening tests for an early understanding of the BMI of the individuals to get an idea of the total rate of the population suffering from obesity or on the verge of developing obesity must be promoted. Franssen et al. (2008) stated that an appropriate assessment of the population having obesity would help in preventing the development of pulmonary diseases or COPD through the provision of interactive interventions and successful physical therapeutic services and providing access to adequate equipment and medication that are used to relieve the conditions associated with obesity [13]. Implementation of educational tools where to get information regarding in the proper diet that must be followed in the general exercise routine that must be integrated into the system of the individuals must also be utilized for derailing the establishment of obesity and improper diet intake.

3. Alternative to lifestyle changes

The promotion of behavioral intervention and promoting changes or alterations in the lifestyle pattern of the individual patient is one of the most acceptable strategies that must be applied to mitigate the problem associated with the development of COPD due to obesity and improper diet intake [1]. Integrating a combination of physical activities along with management of the diet in accordance with the prescribed medicine and surgery would allow the patient to lose a significant amount of weight that would, in turn, relieve the stress on the thoracic region of the body and would prevent the accumulation of fat in the lungs of the patient [23]. Surveillance step follow- up systematic track of the cost-benefits associated with the physical intervention and the health quality progress of the patient in losing weight through the diet control and exercise routine must be critically analyzed to understand the effects that intimation is having towards relieving the symptom of a chronic obstructive pulmonary disease of the patient.

3.1. Visualization of COPD pathogenesis with functional connectivity

Chronic obstructive pulmonary disorder is a complicated and heterogenetic disorder that leads to the development of extensive long problems along with suffocation and breathing issues which leads to the increase in the rate of mortality and significantly impacts the health care delive
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patterns in the environment are significantly associated with the pathogenesis of chronic obstructive pulmonary disorder [28, 31]. Moreover, associated diseases such as obesity and hypertension are also extremely related to the development and the pathogenesis of chronic obstructive pulmonary disorder.

The development of chronic obstructive pulmonary disorder is multifactorial and very complex, and certain measures can be applied for the complete analysis of the pathogenesis of COPD: FEV (forced expiratory volume) which indicates the amount of air that can be forced from the lungs per second. FEV has also been utilized as a potential indicator to measure the presence of certain history of smoking that promotes the establishment of emphysema and enhances the progression of COPD. In previous studies of the evaluation of COPD longitudinally to identify predictive surrogate endpoints (ECLIPSE), they found age and smoking is a critical factor which influence FEV1 reversibility such as decreased in more severe lung disease with symptomatic index after comparing big data covering clinical aspects (i.e., BMI, symptomatic indicators, history of metabolic disorder, smoker, etc.), physiological (i.e., FVC level, FEV¹/VC ratio) and imaging data (i.e., emphysema), interestingly, fat-free mass index (FFMI) no difference between groups [1].

Alqahtani et al. (2020) examined the effect of COVID-19 on COPD patients who had smoking history and conducted data analysis using systemic review and Meta-Analyses (PRISMA) guidelines. Study outcome about connectivity between COPD and infection of Covid -19 shown a low. However, they suggested that smoking is a more vulnerable potential risk in health complications and increased mortality rate cause compared to former and non-smokers [3].

There are several studies that reported the connectivity due to the alteration of the immune system and the development of extensive inflammation in different types of respiratory disorders, for example Alpha-1 Antitrypsin Deficiency (AATD) and cystic fibrosis transmembrane conductance regulator (CFTR) activity which was determined utilize nasal potential difference (NPD) and lower airway potential difference (LAPD) assays. The outcomes indicated that smoking included chronic bronchitis, and dyspnea scores was associated with CFTR dysfunction likely reducing activity of LAPD CFTR activity [7].

In addition, Gramegna et al (2018) reported correlation between Alpha-1 Antitrypsin Deficiency (AATD) and respiratory disorders (i.e., Asthma, bronchiectasis, and COPD). AATD is heterogeneity, likely several mutations in the SERPINA1 gene which encodes for AAT and its deficiency increased severe mortality due to FEV1 impairment which might be associated with cardiometabolic risk as well [15].

4. Impact of metabolic disorder on COPD and its genetic modification

Obesity is a disease that sometimes happens due to excessive eating of fast food, or it can also have occurred because of the genetic factors coming from the parents to the offspring. Obesity causes many problems in which respiratory problems come at the priority list, which is affected by the reason for obesity [9]. Obesity is a disease in which excessive fat gets stored underneath the skin, causing many health problems such as getting type 2 diabetes, having high blood pressure, and some serious respiratory change it to issues which can also result in fatality or death. Chronic obstructive pulmonary disease or COPD is a chronic lung disease that reduces the efficiency of the lungs to work for breathing, and it degrades with growing age or with gaining weight.

The study led by Esteban et al. (2016) demonstrated how the change of physical activity (PA) on COPD during a moderate-to-severe COPD exacerbation (eCOPD) using data collected from clinical and sociodemographic data from medical records, dyspnea, health-related quality of life. It suggests that PA is the strongest predictor of dying or high-risk determinant factor worst PA after eCOPD using their prospective observational cohort study [6, 8].

Obesity and COPD has metabolic similarities: the lung cannot perform with the regular flow as the volume of the lungs is decreased because of the fat which is present underneath the skin with atelectasis and airflow limitation that can result in air trapping. Alqahtani et al. (2020) suggests that obesity is genetic predisposition which can be transferred from the gene of the parents and there can be problems in the time of working hard by the person as of low air transportation because of weight gain in an insignificant way [3].

Recently, it was reported that genetic modification was associated with chronic obstructive pulmonary disease regarding Surfactant protein D (SP-D): SFTPD, encoding gene involved innate immunity and metabolism of surfactant. In addition, gene expression of SFTPD detected in various tissue tropism for example respiratory system, digestive system, reproductive system, circulatory system, gland and more. Polymorphism of SFTPF interacted with metabolic disorders such as atherosclerosis, Diabetes, and obesity [30]

This can be better understood in the follow-up study including functional, physiological, and molecular imaging assessment which reflect health stage of lung in patient who are suffering COPD and further monitoring process to prevent of lung cancer following by smoking survey and molecular imaging screening such as CT scan and genetic alteration combined with in situ protein array, microarray, biochemical analysis of inflammatory cytokines, and molecular diagnostic in histological analysis. Simultaneously, this can be determined by understanding the quality of life the person is having and by doing the 6-minute walking distance test, which shows the ability of the person to work. Doses can be applied to make these corrections, but it cannot be cured fully [9]. It suggests that obesity has mixed effects and can be the reason for the possible cause of asthma and respiratory complications which may have synergic effect to mortality and health quality.

4.1. Pattern of comorbidity pairing with metabolic disorder.

Respiratory problems are still a multifactorial complication of health to the human being as it interrupts the oxygen supply of the body and is more vulnerable to various infectious diseases. Obesity is a potential silent risk for chronic obstructive pulmonary disease (COPD). In previous studies, Obesity (BMI >40) appears to cause risk and prevalence to trigger respiratory diseases with metabolism and physical activity limitation [23, 31, 34]. Obesity can itself cause a variety of health risks like anxiety, depression and sleeping issues, but in cases of respiratory problems, the excessive formation of fat, chronic venous insufficiency, or vein thrombosis prevents the homeostasis of the body from having a healthy life ahead. Some of the diseases, hypertension, refluxes and cardiovascular heart disorder which can be pointed out because of the factors of obesity on COPD are that these people are very prone to hypoxia development due to environmental factors and stress as potential high-risk.

Many people have the condition of asthma because of obesity. Some patients also suffer from high blood pressure, and some suffer from diabetes problems because of obesity. Diabetes is a huge problem for everyone as it prevents the body from getting recovered in many ways. Pulmonary atelectasis is also an undesired problem that is associated with obesity in lung diseases [31]. This is a condition where the lungs cannot perform to their fullest and as an increase in vascular resistance and can have infectious complications. Alqahtani (2020) stated that it has also been seen that some patients were suffering from acute respiratory failure, which is a serious thing to look into [3]. Sleep apnea syndrome and advanced-stage heart failure due to obesity causing high blood pressure is also a significant disease. With all of these diseases, high body mass index is also a disease and a problem that should be taken care of [31].

5. Future Perspectives

Environmental Stressors (e.g., biological, chemical, physical, and emotional stress) induce health burdens in the modern lifestyle owing to urbanization, globalization, and climate change. Many people underestimated how stress can negatively affect balance of health such as mental and metabolic health complications. Recently, one of the environmental stressors, for example, air pollution, causes a diversity of mental and physical health problems: heart disease, anxiety, hypertension, stroke, diabetes, obesity, asthma, and COPD. Environmental stress can alter health conditions and interact with the immune system, hormonal balance, endocrine system, which may affect human behaviors, for example anxiety, and metabolic syndrome: Obesity, diabetes, inflammatory bowel disease and unhealthy eating habits. Environmental Stressor is attributed to COPD pathogenesis as a molecular modifier and trigger among molecular network pathways which may synergically interact with existing the human's chronic diseases that exaggerate intervention of metabolism between hormonal and neuronal circuits. In the future study, multidimensional molecular based risk assessment skills is worth to detect gene alteration effectively in terms of single nucleotide polymorphism (SNP) using omics platform (i.e., metabolomic, genomics, epigenomics, pharmacogenomics, and nutrigenomics). Chromosomal mapping and visualization of polymorphism pattern using biopsy of patient could be beneficial to prevent early interaction between human chronic disease (i.e., COPD) and metabolic disorder (i.e., Obesity, diabetes, hypertension, sleep disorder, Bowel disease and hypertension) covering monitoring and crosslinking with surveillance follow-up study in the molecular based diagnostic lead to improve quality of patient care.

6. Conclusion

Obesity is a growing health burden with concern of health cost that is critically associated with the development of pulmonary diseases and chronic obstructive pulmonary disorders, which is leading causes of mortality during Covid-19 pandemic around the global which predisposed with variety of health risks in secondary of chronic disorders. A proper assessment such as molecular diagnostic following body mass index of the individual members of the global population must be implemented in the health surveillance systems and the health record update to understand the effects of obesity on the pulmonary system of human beings with or without smoking record. Interventional screening strategy focus on target molecules using genomics based-diagnostic tools combined with education like advocacy of

health behavioral approach play a key role in counteracting disease risk related to environmental exposome and stress. Lifestyle changes of the patients who were suffering from metabolic disorder likely obesity could be implemented with a patient care package with stress management and diet recipe at the clinic level. Metabolic disorders should excel pulmonary disorders associated with quality of life, and health disability. However, it is possible to mitigate the extensive health cost and provide a more affordable action plan integrated with a wider spectrum of preventive measures including knowledge-based and cognitive-based risk prevention combined with visualization of the outcomes like stress endurance test, mindful exercise, practice diet restriction, and weight management. Disease prevention supplemented with physical exercise is beneficial and exploring new biomarkers can predict exposure risk by understanding nutrigenomics with molecular dynamics which may interact with metabolites- driven tissue damage, restructuring, and remodeling. It would be beneficial for those who were suffering from obesity-induced COPD or metabolic disease-driven lung disease with nutrient-based precision care with molecular imaging.

Compliance with ethical standards

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Disclosure of conflict of interest

The Authors declare no conflicts of interest.

References

- [1] Agusti A, Calverley PM, Celli B, Coxson HO, Edwards LD, Lomas DA, MacNee W, Miller BE, Rennard S, Silverman EK, Tal-Singer R, Wouters E, Yates JC, Vestbo J. Evaluation of COPD Longitudinally to Identify Predictive Surrogate Endpoints (ECLIPSE) investigators. Characterisation of COPD heterogeneity in the ECLIPSE cohort. *Respiratory research*. 2010; 11(1): 122.
- [2] Alcázar-Navarrete B, Trigueros JA, Riesco JA, Campuzano A, Pérez J. Geographic variations of the prevalence and distribution of COPD phenotypes in Spain: "the ESPIRAL-ES study". *International journal of chronic obstructive pulmonary disease*. 2018; 13: 1115–1124.
- [3] Alqahtani JS, Oyelade T, Aldhahir AM, Alghamdi SM, Almehmadi M, Alqahtani AS, Quaderi S, Mandal S, Hurst JR. Prevalence, Severity and Mortality associated with COPD and Smoking in patients with COVID-19: A Rapid Systematic Review and Meta-Analysis. *PloS one*. 2020; 15(5): e0233147.
- [4] Billingsley H, Rodriguez-Miguel P, Del Buono MG, Abbate A, Lavie CJ, Carbone S. Lifestyle Interventions with a Focus on Nutritional Strategies to Increase Cardiorespiratory Fitness in Chronic Obstructive Pulmonary Disease, Heart Failure, Obesity, Sarcopenia, and Frailty. *Nutrients*. 2019; 11(12): 2849.
- [5] Collins PF, Elia M, Stratton RJ. Nutritional support and functional capacity in chronic obstructive pulmonary disease: a systematic review and meta-analysis. *Respirology (Carlton, Vic.)*. 2013; 18(4): 616–629.
- [6] Dixon AE, Pratley RE, Forgione PM, Kaminsky DA, Whittaker-Leclair LA, Griffes LA, Garudathri J, Raymond D, Poynter ME, Bunn JY, Irvin CG. Effects of obesity and bariatric surgery on airway hyperresponsiveness, asthma control, and inflammation. *The Journal of allergy and clinical immunology*. 2011; 128(3): 508–15.e152.
- [7] Eisner MD, Blanc PD, Sidney S, Yelin EH, Lathon PV, Katz PP, Tolstykh I, Ackerson L, Iribarren C. Body composition and functional limitation in COPD. *Respiratory research*. 2007; 8(1): 7.
- [8] Esteban C, Garcia-Gutierrez S, Legarreta MJ, Anton-Ladislao A, Gonzalez N, Lafuente I, COPD group, IRYSS. One-year mortality in COPD after an exacerbation: the effect of physical activity changes during the event. *COPD: Journal of Chronic Obstructive Pulmonary Disease*. 2016; 13(6): 718-725.
- [9] Ferreira IM, Brooks D, White J, Goldstein R. Nutritional supplementation for stable chronic obstructive pulmonary disease. *The Cochrane database of systematic reviews*. 2012; 12: CD000998.
- [10] Finkelstein EA, Khavjou OA, Thompson H, Trogdon JG, Pan L, Sherry B, Dietz W. Obesity and Severe Obesity Forecasts Through 2030. *American Journal of Preventive Medicine*. 2012; 42(6): 563–570.

- [11] Fitzgerald MP, Hennigan K, O’Gorman CS, McCarron L. Obesity, diet and lifestyle in 9-year-old children with parentally reported chronic diseases: findings from the Growing Up in Ireland longitudinal child cohort study. *Irish Journal of Medical Science*. 2019; 188(1): 29–34.
- [12] Franssen FME, O’Donnell DE, Goossens GH, Blaak EE, Schols AMWJ. 2008 Obesity and the lung: 5. Obesity and COPD Thorax. 2019; 63(12): 1110–1117.
- [13] GBD 2017 DALYs and HALE Collaborators. Global, regional, and national disability-adjusted life-years (DALYs) for 359 diseases and injuries and healthy life expectancy (HALE) for 195 countries and territories, 1990-2017: a systematic analysis for the Global Burden of Disease Study 2017. *Lancet (London, England)*. 2018; 392(10159): 1859–1922.
- [14] Hanson C, Rutten EP, Wouters EF, Rennard S. Influence of diet and obesity on COPD development and outcomes. *International journal of chronic obstructive pulmonary disease*. 2014; 9: 723–733.
- [15] James BD, Jones AV, Trethewey RE, Evans RA. Obesity and metabolic syndrome in COPD: Is exercise the answer? *Chronic respiratory disease*. 2018; 15(2): 173–181.
- [16] Jones RL, Nzekwu MM. The effects of body mass index on lung volumes. *Chest*. 2006; 130(3): 827–833.
- [17] Kim V, Criner GJ. Chronic bronchitis and chronic obstructive pulmonary disease. *American journal of respiratory and critical care medicine*. 2013; 187(3): 228–237.
- [18] Lainscak M, von Haehling S, Doehner W, Sarc I, Jeric T, Zihelr K, Kosnik M, Anker SD, Suskovic S. Body mass index and prognosis in patients hospitalized with acute exacerbation of chronic obstructive pulmonary disease. *Journal of cachexia, sarcopenia and muscle*. 2011; 2(2): 81–86.
- [19] Mafort TT, Rufino R, Costa CH, Lopes AJ. Obesity: systemic and pulmonary complications, biochemical abnormalities, and impairment of lung function. *Multidisciplinary respiratory medicine*. 2016; 11: 28.
- [20] McDonald VM, Gibson PG, Scott HA, Baines PJ, Hensley MJ, Pretto JJ, Wood LG. Should we treat obesity in COPD? The effects of diet and resistance exercise training. *Respirology (Carlton, Vic.)*. 2016; 21(5): 875–882.
- [21] McLoughlin RF, McDonald VM, Gibson PG, Scott HA, Hensley MJ, MacDonald-Wicks L, Wood LG. The Impact of a Weight Loss Intervention on Diet Quality and Eating Behaviours in People with Obesity and COPD. *Nutrients*. 2017; 9(10): 1147.
- [22] Pellegrino R, Gobbi A, Antonelli A, Torchio R, Gulotta C, Pellegrino GM, Dellacà R, Hyatt RE, Brusasco V. Ventilation heterogeneity in obesity. *Journal of applied physiology (Bethesda, Md.)*. 2014; 116(9): 1175–1181.
- [23] Pelosi P, Croci M, Ravagnan I, Tredici S, Pedoto A, Lissoni A, Gattinoni L. The effects of body mass on lung volumes, respiratory mechanics, and gas exchange during general anesthesia. *Anesthesia and analgesia*. 1998; 87(3): 654–660.
- [24] Salome CM, Munoz PA, Berend N, Thorpe CW, Schachter LM, King GG. Effect of obesity on breathlessness and airway responsiveness to methacholine in non-asthmatic subjects. *International journal of obesity*. 2008; (2005); 32(3): 502–509.
- [25] Schachter LM, Salome CM, Peat JK, Woolcock AJ. Obesity is a risk for asthma and wheeze but not airway hyperresponsiveness. *Thorax*. 2001; 56(1): 4–8.
- [26] Scoditti E, Massaro M, Garbarino S, Toraldo DM. Role of diet in chronic obstructive pulmonary disease prevention and treatment. *Nutrients*. 2019; 11(6): 1357.
- [27] Sin DD, Jones RL, Man SF. Obesity is a risk factor for dyspnea but not for airflow obstruction. *Archives of internal medicine*. 2002; 162(13): 1477–1481.
- [28] Spelta F, Pasini AF, Cazzoletti L, Ferrari M. Body weight and mortality in COPD: focus on the obesity paradox. *Eating and weight disorders-studies on anorexia, bulimia and obesity*. 2018; 23(1): 15-22.
- [29] Standards for the diagnosis and care of patients with chronic obstructive pulmonary disease. American Thoracic Society. *American Journal of Respiratory and Critical Care Medicine*. 1995; 152(5 Pt 2): S77–S121.
- [30] Vozoris NT, O’Donnell DE. Prevalence, risk factors, activity limitation and health care utilization of an obese, population-based sample with chronic obstructive pulmonary disease. *Canadian respiratory journal*. 2012; 19(3): e18–e24.
- [31] Wang C, Zhou J, Wang J, Li S, Fukunaga A, Yodoi J, Tian H. Progress in the mechanism and targeted drug therapy for COPD. *Signal transduction and targeted therapy*. 2020; 5(1): 248.

- [32] Zerah F, Harf A, Perlemuter L, Lorino H, Lorino AM, Atlan G. Effects of obesity on respiratory resistance. *Chest*. 1993; 103(5): 1470–1476.
- [33] Zewari S, Hadi L, van den Elshout F, Dekhuijzen R, Heijdra Y, Vos P. Obesity in COPD: Comorbidities with Practical Consequences? *COPD*. 2018; 15(5): 464–471.
- [34] Gramegna A, Stefano Aliberti S, Marco Confalonierin M, Angelo Corsico A, Luca Richeldi L, Carlo Vancheri C, Francesco Blasi F. Alpha-1 antitrypsin deficiency as a common treatable mechanism in chronic respiratory disorders and for conditions different from pulmonary emphysema? A commentary on the new European Respiratory Society statement. *Multidisciplinary Respiratory Medicine*. 2018; 13: 39.
- [35] Dransfield MT, Wilhelm AM, Flanagan B, Courville C, Tidwell SL, Raju SV, Amit Gaggar A, Chad Steele C, Tang LP, Bo Liu B, Rowe SM. Acquired cystic fibrosis transmembrane conductance regulator dysfunction in the lower airways in COPD. *Chest*. 2013; 144(2): 498-506.
- [36] Vaughan A, Frazer ZA, Hansbro PM, Yang IA. COPD and the gut-lung axis: the therapeutic potential of fibre. *J Thorac Dis*. 2019; 11(17): S2173-S2180.
- [37] Sorensen GL. Surfactant Protein D in Respiratory and Non-Respiratory Diseases. *Front. Med*. 5:18.
- [38] Suratt BT. Weight Gain and Lung Disease: The Vagary of Body Mass Index and the Dilemma of the Obese Smoker. *Am J Respir Crit Care Med*. 2014; 189(3): 240–242.