

Research Progress on Influencing Factors, Mechanisms, and Therapeutic Regimens of Adverse Emotions in COPD Patients

Rong Xiao, Ruicheng Hu*

The First Affiliated Hospital of Hunan Normal University (Hunan Provincial People's Hospital), Changsha, Hunan, China.

How to cite this paper: Rong Xiao, Ruicheng Hu. (2024) Research Progress on Influencing Factors, Mechanisms, and Therapeutic Regimens of Adverse Emotions in COPD Patients. *International Journal of Clinical and Experimental Medicine Research*, 8(1), 1-7.
DOI: 10.26855/ijcemr.2024.01.001

Received: November 8, 2023

Accepted: December 5, 2023

Published: December 30, 2023

***Corresponding author:** Ruicheng Hu, The First Affiliated Hospital of Hunan Normal University (Hunan Provincial People's Hospital), Changsha, Hunan, China.

Abstract

Chronic obstructive pulmonary disease (COPD) is a serious respiratory system disease in China and even the world, which seriously affects patients' health and quality of life. In addition to COPD symptoms, the accompanying anxiety, depression, and other adverse emotions have gradually attracted widespread attention. Based on the summary of previous literature, this article summarizes the influencing factors of adverse emotions in COPD patients, including smoking, chronic pain, activity limitation, drug effect, gender, fatigue, etc. Clinical treatment can be taken through continuous and close observation of the influencing factors of adverse emotions, and timely and effective intervention measures can be taken for high-risk groups. At present, the exact pathogenesis of anxiety and depression in COPD patients is still unclear. It involves multiple complex pathophysiological factors such as hypoxemia and chronic inflammation, which may also include behavioral factors such as active smoking and tobacco addiction, as well as other factors such as social isolation, complications, declined physical function, and frequent re-hospitalization. This study summarizes several mechanisms such as hyperventilation, carbon dioxide retention, hypoxemia, inflammation, immune regulation, cognitive behaviors, and sleep disorders so as to determine the possible mechanisms of anxiety, depression, and other adverse emotions in COPD patients and to assist the clinical search for effective therapeutic targets. Finally, this article summarizes the treatment progress of adverse emotions in COPD patients mainly through antipsychotics and TCM therapy, individualized breathing intervention, and cognitive behavioral therapy.

Keywords

Chronic obstructive pulmonary disease, Adverse emotion, Influencing factor, Mechanism, Treatment, Research progress

Chronic obstructive pulmonary disease (COPD) is a heterogeneous lung condition often triggered by exposure to harmful particles or gases, resulting in lung inflammation characterized by chronic respiratory symptoms (such as breathlessness, cough, and sputum production). It is characterized by persistent (often progressive) airflow obstruction due to abnormalities in the airways (chronic bronchitis, small airway disease) and/or lung parenchyma (emphysema) [1]. Epidemiologically, COPD mortality ranks highest among respiratory diseases in our country and is one of the top three global causes of death, presenting a concerning scenario [2]. Apart from impacting the health and quality of life of patients, COPD, with its protracted course, recurrent exacerbations, and progressive nature, gives rise to numerous psychological and socio-adaptive issues. The primary demographic affected by COPD comprises elderly

individuals, who experience significant declines in physical and cognitive capabilities. These individuals struggle in social interactions, tending to withdraw from societal engagements, leading to a deepening sense of loneliness and social alienation. Consequently, negative emotions like anxiety and depression become more prevalent. Moreover, COPD patients with comorbid anxiety and depression adversely affect their health status, increasing the risk of acute exacerbations, hospital readmissions, and mortality rates [3-6]. Studies indicate that compared to individuals with other chronic illnesses, COPD patients exhibit higher prevalence rates of psychological distress, including anxiety and depression. Overseas literature reports that approximately 10% to 57% of stable COPD patients experience symptoms of depression, with 7% to 50% experiencing anxiety. Among COPD patients requiring long-term oxygen therapy, the prevalence of depression reaches 57%, with 18% experiencing severe depression. These negative emotions worsen as the COPD condition progresses [7]. Domestic literature reports a prevalence of anxiety and depression in COPD ranging between 19.8% to 71.0%, significantly higher than in non-COPD patients [8]. The psychological issues in COPD patients demand attention. This article synthesizes and summarizes the mechanisms, influencing factors, and treatment advancements concerning anxiety and depression comorbidity in COPD patients, aiming to enhance the comprehensive management of clinical COPD.

1. Factors Influencing Adverse Emotions in COPD Patients

1.1 Smoking

Smoking not only stands as a significant risk factor in the onset and progression of COPD but also correlates closely with the emergence of adverse emotions like anxiety and depression. Extensive research confirms smoking as a major risk factor in COPD pathogenesis, and smoking cessation can delay COPD progression while alleviating adverse emotions [9, 10]. Smoking-mediated acetylcholine receptor activation and inflammatory responses form the pathological basis of COPD. During this process, there is an increased secretion of inflammatory factors, inducing pulmonary inflammatory reactions while also triggering neuropathies associated with anxiety and depression [11]. Additionally, smoking-induced oxidative stress leads to abnormal brain and lung function metabolism, and disruption in the secretion of cortisol and serotonin, contributing to the development of anxiety and depression in COPD patients. Some COPD patients attempt to alleviate various negative emotions caused by their symptoms by initiating or increasing smoking behavior. Smoking, by affecting neurons, heightens the body's sensitivity to external stressors, making the occurrence of adverse emotions such as anxiety and depression more likely. Cekerevac et al. suggest that smoking not only increases the risk and severity of COPD but also elevates the incidence of anxiety and depression in COPD patients [12].

1.2 Chronic Pain

Chronic pain caused by COPD is one of the risk factors for anxiety and depression in patients. The longer the duration and the higher the severity of pain, the more it directly leads to decreased sleep quality and reduced physical activity in patients. Those severely affected may even develop aversions to physical activity, which is detrimental to COPD recovery and significantly increases the likelihood of depression and anxiety in patients [13].

1.3 Activity Limitation

The decline in daily life abilities due to activity limitations in COPD patients is a crucial reason for reduced social engagement. Previous studies indicate a noticeable decrease in social participation among COPD patients compared to elderly individuals without COPD. Reduced social engagement leads to increased feelings of loneliness and decreased self-identity, further developing into adverse emotions like anxiety and depression [14].

1.4 Medication Effects

Certain medications used in the treatment of COPD, such as glucocorticoids, can induce anxiety and depression symptoms in patients. This primarily occurs by affecting glucocorticoid receptors in the hippocampal structure of the body, accelerating degeneration and apoptosis of hippocampal neurons, resulting in emotional issues [15].

1.5 Gender

Female COPD patients may be more susceptible to emotional disorders such as anxiety and depression due to factors related to endocrine disruptions, hormonal changes, and a greater need for emotional support and social interaction.

However, some reports suggest that male COPD patients are more prone to these adverse emotions [16-18]. There's also a perspective stating that there might not be a definite connection between gender and the occurrence of anxiety and depression in COPD patients [19]. Presently, there is no unified conclusion regarding the impact of gender on the occurrence of anxiety and depression.

1.6 Fatigue

Current research indicates a fatigue occurrence rate of 17% to 95% in COPD patients [20]. Past studies show that fatigue can lead to acute exacerbations in COPD patients and is associated with their prognosis [21, 22]. Research by Fang Ziyuan et al. suggests that fatigue is prevalent among COPD patients and can increase the risk of COPD acute exacerbations by more than tenfold. It serves as a predictive factor for COPD exacerbations, and clinical assessment of patient fatigue can aid in analyzing COPD conditions [23]. Fatigue is a subjective feeling of discomfort and, besides breathlessness, is one of the most common symptoms in COPD patients. Fatigue symptoms also contribute to the emergence of anxiety and depression in patients.

2. Mechanisms Underlying the Comorbidity of Adverse Emotions in COPD Patients

Currently, the precise pathophysiological mechanisms leading to anxiety and depression in COPD patients remain unclear. It involves multiple complex pathophysiological factors such as hypoxemia, chronic inflammation, behavioral factors like active smoking and tobacco addiction, as well as social isolation, comorbidities, decreased physical function, and frequent rehospitalizations [24].

2.1 Hyperventilation Mechanism

Hyperventilation, where a patient breathes at a rate exceeding metabolic needs, causes a decrease in carbon dioxide levels in the body, leading to respiratory alkalosis. This pattern is common in COPD patients with comorbid anxiety and is a manifestation of respiratory dysfunction [25]. Hyperventilation exacerbates dyspnea and panic attacks in COPD patients, further inducing hypocapnia. Activation of carbon dioxide-sensitive neurons in the body may trigger defensive behaviors and lead to symptoms like anxiety. COPD patients experiencing adverse bodily sensations due to hyperventilation often exhibit increased severity of adverse emotions [26].

2.2 Carbon Dioxide Retention

COPD patients often face issues like dyspnea or respiratory failure. Hypoxia and carbon dioxide retention lead to increased pulmonary arterial pressure, and reduced cardiac pumping ability, causing systemic ischemia and hypoxia. When cerebral perfusion is inadequate, it results in brain damage, which is the fundamental factor for anxiety and depression events in COPD patients. Moreover, organ ischemia induces increased reactive oxygen species production and oxidative stress, neuronal apoptosis, contributing to the onset of depression [27].

2.3 Hypoxemia

Persistent hypoxemia in COPD patients leads to cerebral white matter lesions, similar to those observed in studies focusing on elderly individuals with depression. Additionally, other researchers suggest that sustained hypoxemia impairs cognitive function, and one of the sequelae is depression, positing hypoxemia as a potential factor in inducing depression in patients [28, 29].

2.4 Inflammatory Mechanism

Studies indicate significantly elevated levels of inflammatory factors in COPD patients with comorbid depression. Interleukin-6 (IL-6) plays a crucial role in neurodegenerative diseases, with levels gradually increasing in COPD alone, depression alone, and COPD with depression, suggesting its involvement in the development of depression, possibly through central inflammation processes [30, 31]. Research by Xu et al. suggests a role for C-reactive protein (CRP) in the occurrence of depression in COPD patients [32]. Thus, disrupted levels of inflammatory-related factors may be associated with negative emotions in COPD patients, and the progression of emotions such as anxiety and depression may be mediated through inflammatory mechanisms.

2.5 Immune Regulation Mechanism

Some researchers have confirmed the association between immune response imbalance and the occurrence of adverse emotions like anxiety and depression. Dysregulated immune cell cytokine secretion can promote nervous system disturbances, leading to anxiety and depression. Furthermore, it can mediate adverse emotions through inflammatory reactions [33]. Studies show that physiological processes like adaptive immune responses and T lymphocyte activation play roles in the occurrence of depression in COPD, and severe depression patients exhibit a significant decrease in peripheral blood T lymphocytes [34].

2.6 Cognitive-Behavioral Mechanism

COPD patients experience varying degrees of respiratory limitations, making them more sensitive to sensations like dyspnea, sometimes interpreting normal physiological phenomena as dangerous signals, resulting in anxiety or panic attacks. Additionally, the presence of psychological symptoms is often associated with reduced self-efficacy, which may lower disease-coping abilities, causing self-anxiety and panic. Understanding of COPD disease also influences the occurrence of anxiety and depression symptoms in patients. Research by Zhou Xiaoping et al. indicates that individuals with higher education levels are more prone to anxiety and depression because they can access various sources of COPD-related information but have limited knowledge, leading to misconceptions about the disease and worsening anxiety and depression levels [35].

2.7 Sleep Disorders

Past studies show that over 70% of COPD patients have sleep disorders, possibly related to nocturnal desaturation. The co-occurrence of sleep disorders further exacerbates anxiety and depression symptoms in COPD patients [36].

3. Progress in the Treatment of Adverse Emotions in COPD Patients

COPD patients often find themselves in a vicious cycle of dyspnea, decreased exercise capacity, reduced mobility, and social isolation. Anxiety and depression are integral components of this cycle. Unfortunately, COPD patients with comorbid adverse emotions seldom receive relevant treatment for anxiety or depression. Studies indicate that only one-third of COPD patients with combined anxiety and depression receive treatment [37]. Existing experimental results suggest that untreated anxiety and depression are associated with poor patient compliance, reduced quality of life, increased mortality rates, increased hospital admissions and readmissions, prolonged hospital stays, and subsequent increases in healthcare system costs. Hence, early identification of adverse emotions in patients and effective management are crucial in enhancing patient compliance, and quality of life, reducing the risk of acute exacerbations, and readmission rates [38].

Pharmacotherapy is one of the treatment modalities for COPD patients with comorbid anxiety and depression. However, its effectiveness is contentious and often accompanied by side effects. Administering appropriate antipsychotic medications can rapidly improve anxiety and depression symptoms in COPD patients. Yet, some patients refuse medication due to concerns about dependence or potential adverse reactions, exacerbating their anxiety, depression, or other emotions. Studies indicate a relationship between the dosage of psychotropic drugs and the occurrence of acute respiratory failure in COPD patients, restricting the clinical use of antipsychotics in COPD patients with comorbid anxiety and depression. More well-designed clinical controlled trials are needed to supplement whether antipsychotic medications are widely applicable for improving and alleviating adverse emotions in COPD patients [39, 40]. Traditional Chinese medicine has made considerable progress in treating COPD with comorbid anxiety and depression. Through the analysis of COPD syndrome differentiation, syndrome elements, according to the pathogenesis and medication laws, help alleviate the anxiety and depression symptoms in patients. Research suggests that Chaihu Shugan San (Bupleurum Relieving Liver Formula) can improve anxiety and depression by regulating the neuroendocrine system and antioxidative stress mechanisms [41].

Individualized respiratory interventions can improve anxiety and depression symptoms in COPD patients by ameliorating their dyspnea [42]. Comprehensive pulmonary rehabilitation can reduce anxiety and depression symptoms in COPD patients in the short term. However, Grosbois et al. argue that this form of rehabilitation only improves COPD patients' respiratory symptoms, and its effectiveness in improving negative emotions remains unclear [43].

Cognitive Behavioral Therapy (CBT) is a psychological approach that identifies and evaluates patients' negative emotions and corrects their maladaptive cognitions, thereby altering beliefs and behaviors, helping patients reconstruct cognitive structures, eliminating adverse emotions, and behaviors, aiding in enhancing patients' self-efficacy

and motivating them to manage their physical conditions, thereby improving their quality of life [44, 45]. Meta-analyses demonstrate that CBT has good effects in alleviating depression in patients with diabetes, breast cancer, and enhancing their quality of life [46, 47]. Relevant evidence suggests that CBT might be the preferred choice for patients with psychological health problems, and there are reports domestically and abroad of applying CBT to COPD patients. A series of psychological treatment plans, including CBT, can improve anxiety and depression emotions in COPD patients, serving as adjunctive therapy and medication substitution for treating COPD with comorbid anxiety and depression. Studies show that even implementing brief CBT can help COPD patients with comorbid anxiety and depression to improve COPD symptoms like dyspnea and anxiety and depression symptoms. However, there is currently no unified standard regarding the optimal duration for administering CBT. Combining CBT with comprehensive pulmonary rehabilitation interventions can offer greater benefits to COPD patients with comorbid anxiety and depression in relieving COPD symptoms and improving anxiety and depression [48].

4. Summary and Outlook

COPD is currently one of the top three causes of death globally, with a high incidence among the elderly population. The situation is concerning as it often leads to persistent illness, acute exacerbations, and poses a significant burden on families and society. A considerable proportion of COPD patients experience adverse emotions like anxiety and depression, which are crucial factors contributing to prolonged illness and a high mortality rate among these patients. Current research indicates that the occurrence of anxiety and depression in COPD might be related to factors such as smoking, chronic pain, limited physical activity, medication effects, gender, fatigue, hyperventilation, CO₂ retention, hypoxemia, oxidative stress, inflammatory responses, immune dysregulation, cognitive behaviors, and sleep disorders. Treatment plans for COPD combined with anxiety and depression are continuously evolving, but existing clinical guidelines do not provide conclusive recommendations for treating COPD with comorbid adverse emotions.

In clinical practice, it is essential to actively screen for adverse emotions when COPD patients exhibit changes in their psychological state. Further assessment is necessary for those with positive screening results to clarify the condition. Once anxiety and depression are identified, it's crucial to promptly provide appropriate and reasonable treatment plans. However, various factors such as patients' lack of relevant knowledge, patient concealment of anxiety and depression symptoms, inability to establish trust between patients and healthcare professionals, patients' misunderstanding of medical behaviors, lack of standardized diagnostic methods for COPD with comorbid anxiety and depression, and uncertainty regarding the efficacy of antipsychotic medications contribute to several issues in treating COPD combined with anxiety and depression. Additionally, limited psychological treatment resources in some patient communities result in the inability to receive timely and appropriate psychological interventions, leading to the continuous spread of anxiety and depression emotions. Given the rapid development of information technology, exploring psychological support models based on internet technology might be a worthwhile and breakthrough intervention to consider.

References

- [1] Global Initiative for Chronic Obstructive Lung Disease. Global Strategy for the Diagnosis, Management and Prevention of Chronic Obstructive Pulmonary Disease (2024 Report) [EB/OL]. [2024-11-12]. <https://goldcopd.org/2024-gold-reports/>.
- [2] Celli BR, Wedzicha JA. Update on Clinical Aspects of Chronic Obstructive Pulmonary Disease [J]. *N Engl J Med*, 2019, 381(13):1257-1266. doi: 10.1056/NEJMra1900500.
- [3] Naberhaus T. Chronic Obstructive Pulmonary Disease, Part 2: A Review of Pharmacotherapy Options [J]. *Sr Care Pharm*, 2023, 38(7):266-275. doi: 10.4140/TCP.n.2023.266.
- [4] Lin FL, Yeh ML, Lai YH, et al. Two-month breathing-based walking improves anxiety, depression, dyspnoea and quality of life in chronic obstructive pulmonary disease: A randomised controlled study [J]. *J Clin Nurs*, 2019, 28(19-20):3632-3640. doi: 10.1111/jocn.14960. Epub 2019 Jun 28.
- [5] Liu, Y., Tian, X., Guo, X., et al. Investigation of Anxiety and Depression in Patients with Chronic Obstructive Pulmonary Disease. *Chinese Journal of Respiration and Critical Care Medicine*, 2020, 19(5): 425-429. DOI: 10.7507/1671-6205.202001049.
- [6] You, Z., Wang, G. Assessment and Countermeasures for Anxiety and Depression in Chronic Obstructive Pulmonary Disease. *Chinese Journal of Practical Internal Medicine*, 2020, 40(10): 805-809. DOI: 10.19538/j.nk2020100104.
- [7] Yohannes AM, Kaplan A, Hanania NA. Anxiety and depression in chronic obstructive pulmonary disease: recognition and management [J]. *Cleve Clin J Med*, 2018, 85(Suppl 1): S11-S18. doi: 10.3949/ccjm.85.s1.03.
- [8] Qi, Y. Application of Psychological Nursing in Patients with Chronic Obstructive Pulmonary Disease Complicated with Anxiety

- and Depression. *Nursing Research*, 2016, 30(36): 4599-4600. DOI: 10.3969/j.issn.1009-6493.2016.36.044.
- [9] Au Yeung SL, Li AM, He B, et al. Association of smoking, lung function and COPD in COVID-19 risk: a two-step Mendelian randomization study [J]. *Addiction*, 2022, 117(7):2027-2036. doi: 10.1111/add.15852. Epub 2022 Mar 7.
- [10] Chang JT, Meza R, Levy DT, et al. Prediction of COPD risk accounting for time-varying smoking exposures [J]. *PLoS One*, 2021, 16(3):e0248535. doi: 10.1371/journal.pone.0248535.
- [11] Yu, Y., Liu, M. Analysis of Risk Factors for Anxiety and Depression in Elderly Patients with Chronic Obstructive Pulmonary Disease. *Chinese Journal of Modern Medicine*, 2019, 29(21): 65-70. DOI: 10.3969/j.issn.1005-8982.2019.21.013.
- [12] Bugajski A, Morgan H, Wills W, et al. Anxiety and Depressive Symptoms in Patients with COPD: Modifiable Explanatory Factors [J]. *West J Nurs Res*, 2023, 45(4):316-326. doi: 10.1177/01939459221129949. Epub 2022 Oct 16.
- [13] Shibata M, Ohara T, Hosoi M, et al. Emotional Loneliness Is Associated with a Risk of Dementia in a General Japanese Older Population: The Hisayama Study [J]. *J Gerontol B Psychol Sci Soc Sci*, 2021, 76(9):1756-1766. doi: 10.1093/geronb/gbaa196.
- [14] Liu, Q., Li, F. Investigation and Analysis of Anxiety and Depression in Patients with Chronic Obstructive Pulmonary Disease. *Modern Hospitals*, 2019, 19(6): 933-936. DOI: 10.3969/j.issn.1671-332X.2019.06.045.
- [15] Lian, C., Zhang, J. Investigation of Anxiety and Depression in Hospitalized Patients with Chronic Obstructive Pulmonary Disease and Related Influencing Factors. *Chinese Journal of Primary Medicine and Pharmacy*, 2016, 23(8): 1126-1129. DOI: 10.3760/cma.j.issn.1008-6706.2016.08.002.
- [16] Wang, R., Xu, J., Liu, H. Analysis of Factors Related to Emotional Disorders in Patients with Chronic Obstructive Pulmonary Disease in Stable Periods. *Chinese Journal of Medicinal Guide*, 2016, 16(4): 463-466. DOI: 10.11655/zgywylc2016.04.003.
- [17] de Miguel-Diez J, Lopez-de-Andres A, Jimenez-Garcia R, et al. National Trends in Prevalence of Depression in Men and Women with Chronic Obstructive Pulmonary Disease Hospitalized in Spain, 2016-2020 [J]. *J Clin Med*, 2022, 11(21):6337. doi: 10.3390/jcm11216337.
- [18] Berman AR. Management of patients with end-stage chronic obstructive pulmonary disease [J]. *Prim Care*, 2011, 38(2):277-97, viii-ix. doi: 10.1016/j.pop.2011.03.008.
- [19] Ding, J. Analysis of Factors Related to Anxiety and Depression in Patients with Chronic Obstructive Pulmonary Disease. *Journal of Clinical Pulmonary Medicine*, 2018, 23(4): 690-693. DOI: 10.3969/j.issn.1009-6663.2018.04.029.
- [20] Ebadi Z, Goërtz YMJ, Van Herck M, et al. The prevalence and related factors of fatigue in patients with COPD: a systematic review [J]. *Eur Respir Rev*, 2021, 30(160):200298. doi: 10.1183/16000617.0298-2020.
- [21] Gruet M. Fatigue in Chronic Respiratory Diseases: Theoretical Framework and Implications for Real-Life Performance and Rehabilitation [J]. *Front Physiol*, 2018, 9:1285. doi: 10.3389/fphys.2018.01285.
- [22] Global Initiative for Chronic Obstructive Lung Disease. Global Strategy for the Diagnosis, Management and Prevention of Chronic Obstructive Pulmonary Disease (2022 Report) [EB/OL]. [2021-11-22]. <https://goldcopd.org/2022-gold-reports-2/>.
- [23] Fang, Z., Li, X., Yang, X., et al. Prospective Cohort Study on the Impact of Fatigue on Acute Exacerbation in Patients with Chronic Obstructive Pulmonary Disease. *Chinese Journal of General Practice*, 2023, 26(3): 287-292. DOI: 10.12114/j.issn.1007-9572.2022.0342.
- [24] Volpato E, Toniolo S, Pagnini F, et al. The Relationship Between Anxiety, Depression and Treatment Adherence in Chronic Obstructive Pulmonary Disease: A Systematic Review [J]. *Int J Chron Obstruct Pulmon Dis*, 2021, 16:2001-2021. doi: 10.2147/COPD.S313841.
- [25] Kawachi S, Fujimoto K. Efficacy of tiotropium and olodaterol combination therapy on dynamic lung hyperinflation evaluated by hyperventilation in COPD: an open-label, comparative before and after treatment study [J]. *Int J Chron Obstruct Pulmon Dis*, 2019, 14:1167-1176. doi: 10.2147/COPD.S201106. PMID: 31213796.
- [26] Li, G., Wang, J., Wang, M., et al. Effects of Daytime Hypersomnia and Subjective Decline in Sleep Quality on Neuro-Psychological Characteristics of Elderly Patients with Obstructive Sleep Apnea-Hypopnea Syndrome. *Jiangsu Medicine*, 2022, 48(3): 237-242. DOI: 10.19460/j.cnki.0253-3685.2022.03.005.
- [27] Boukhenouna S, Wilson Ma, Bahmed K, et al. Reactive Oxygen Species in Chronic Obstructive Pulmonary Disease [J]. *Oxid Med Cell Longev*, 2018, 2018:5730395. doi: 10.1155/2018/5730395.
- [28] Zuberi FF, Zuberi BF, Ali FS, et al. Muscle weakness assessment in non-hypoxemic COPD out-patients at tertiary care hospitals[J]. *Pak J Med Sci*, 2021, 37(2):536-542. doi: 10.12669/pjms.37.2.3127. PMID: 33679946.
- [29] Rivera PM, Proppe CE, Beltran E, et al. Acute Effects of Local Ischemic Hypoxia and Systemic Hypoxemia on Neuromuscular and Cognitive Function [J]. *High Alt Med Biol*, 2022, 23(1):18-25. doi: 10.1089/ham.2021.0096. Epub 2021 Dec 21.
- [30] Yohannes AM, Kaplan A, Hanania NA. Anxiety and depression in chronic obstructive pulmonary disease: recognition and management [J]. *Cleve Clin J Med*, 2018, 85(Suppl 1): S11-S18. doi: 10.3949/ccjm.85.s1.03.
- [31] Beurel E, Toups M, Nemeroff CB. The Bidirectional Relationship of Depression and Inflammation: Double Trouble [J]. *Neuron*, 2020, 107(2):234-256. doi: 10.1016/j.neuron.2020.06.002. Epub 2020 Jun 17.

- [32] Xu K, Li X. Risk factors for depression in patients with chronic obstructive pulmonary disease [J]. *Med Sci Monit*, 2018, 24: 1417-1423. doi: 10.12659/msm.904969.
- [33] Drevets WC, Wittenberg GM, Bullmore ET, et al. Immune targets for therapeutic development in depression: towards precision medicine [J]. *Nat Rev Drug Discov*, 2022, 21(3):224-244. doi: 10.1038/s41573-021-00368-1. Epub 2022 Jan 17.
- [34] Dudek KA, Dion-Albert L, Kaufmann FN, et al. Neurobiology of resilience in depression: immune and vascular insights from human and animal studies [J]. *Eur J Neurosci*, 2021, 53(1):183-221. doi: 10.1111/ejn.14547. Epub 2019 Sep 13.
- [35] Zhou, X.P., Fang, R.H. Survey and Analysis of Anxiety and Depression in Patients with Chronic Obstructive Pulmonary Disease in General Wards. *Chinese Journal of General Practice*, 2022, 20(6): 1003-1006. DOI: 10.16766/j.cnki.issn.1674-4152.002510.
- [36] Gulibakangmu, A., Abdusalamu, A., Ma, R., et al. Influence of Sleep Disorders on Anxiety and Depression Status and Short-Term Prognosis in Elderly Patients with Acute Exacerbation of Chronic Obstructive Pulmonary Disease. *Chinese Journal of Clinical Pulmonary Medicine*, 2022, 27(12): 1882-1885. DOI: 10.3969/j.issn.1009-6663.2022.12.019.
- [37] Ni, X.Q., Gao, Y.L., Li, Z.H. Effects of Zero-Defect Nursing Services on Anxiety and Depression Scores, Tolerance, and Forced Expiratory Volume in 1 Second in COPD Patients with Respiratory Failure. *Modern Medicine*, 2020, 48(2): 288-291. DOI: 10.3969/j.issn.1671-7562.2020.02.031.
- [38] Pollok J, Van Agteren JE, Esterman AJ, et al. Psychological therapies for the treatment of depression in chronic obstructive pulmonary disease [J]. *Cochrane Database Syst Rev*, 2019, 3(3):CD012347. doi: 10.1002/14651858.CD012347.pub2.
- [39] Ji, X.Q., Zhao, Y.X., Geng, Y., et al. The Impact of Diversified Nursing on Pulmonary Function and Psychological Status in COPD Patients with Lung Cancer Undergoing Chemotherapy. *Qilu Nursing Journal*, 2022, 28(13): 51-53. DOI: 10.3969/j.issn.1006-7256.2022.13.015.
- [40] Yohannes AM, Jin JW, Kunik ME. Benefit-Risk Assessment of Psychotropic Drugs in Older Patients with Chronic Obstructive Pulmonary Disease [J]. *Drugs Aging*, 2022, 39(5):323-332. doi: 10.1007/s40266-022-00935-0. Epub 2022 Apr 19.
- [41] Wu, P.Z., Liang, X.X., Wang, S.L. Screening of Tryptophan 2,3-Dioxygenase Inhibitors in Chaihu Shugan Powder and Study on Antidepressant Effects. *Chinese Herbal Medicines*, 2023, 54(9): 2812-2821. DOI: 10.7501/j.issn.0253-2670.2023.09.014.
- [42] Qian MYY, Politis J, THOMPSON M, et al. Individualized breathlessness interventions may improve outcomes in patients with advanced COPD [J]. *Respirology*, 2018, 23(12):1146-1151. doi: 10.1111/resp.13324. Epub 2018 May 15.
- [43] Grosbois JM, Gephine S, Kyheng M, et al. Physical and affective components of dyspnoea are improved by pulmonary rehabilitation in COPD[J]. *BMJ Open Respir Res*, 2022, 9(1):e001160. doi: 10.1136/bmjresp-2021-001160.
- [44] Mathisen TF, Rosenvinge JH, Friberg O, et al. Is physical exercise and dietary therapy a feasible alternative to cognitive behavior therapy in treatment of eating disorders? A randomized controlled trial of two group therapies [J]. *Int J Eat Disord*, 2020, 53(4):574-585. doi: 10.1002/eat.23228. Epub 2020 Jan 16.
- [45] Stefan S, Cristea IA, Szentagotai Tatar A, et al. Cognitive-behavioral therapy (CBT) for generalized anxiety disorder: Contrasting various CBT approaches in a randomized clinical trial [J]. *J Clin Psychol*, 2019, 75(7):1188-1202. doi: 10.1002/jclp.22779. Epub 2019 Apr 20.
- [46] Wu, Y., Duan, H.W., Chen, X. Meta-Analysis of Cognitive Behavioral Therapy for Improving Depression and Blood Sugar in Diabetic Patients. *Journal of Nursing*, 2018, 33(3): 23-27. DOI: 10.3870/j.issn.1001-4152.2018.03.023.
- [47] Ye M, Du K, Zhou J, et al. A meta-analysis of the efficacy of cognitive behavior therapy on quality of life and psychological health of breast cancer survivors and patients[J]. *Psychooncology*, 2018, 27(7):1695-1703. doi: 10.1002/pon.4687. Epub 2018 Mar 26.
- [48] Singh SJ, Baldwin MM, Daynes E, et al. Respiratory sequelae of COVID-19: pulmonary and extrapulmonary origins, and approaches to clinical care and rehabilitation [J]. *Lancet Respir Med*, 2023, 11(8):709-725. doi: 10.1016/S2213-2600(23)00159-5. Epub 2023 May 19.