Incidence of Anxiety and Depression in Patients with Chronic Obstructive Pulmonary Disease: A Meta-Analysis

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Abstract

Objective: To systematically evaluate the incidence of COPD with anxiety and depression in the past 5 years.

Methods: The databases of CNKI, Wanfang, VIP, CBM, PubMed, WebofScience, TheCochraneLibrary and EMBase were searched by computer. The study type was cross-sectional study or other types of study that included baseline data. Outcome indicators included the incidence of anxiety or depression; The cross-sectional study evaluation scale recommended by AHRQ was used to evaluate the quality of the included literature, and StataSE 16 was used to complete the meta-analysis.

Results: A total of 35 literatures were included, including 27 Chinese literatures and 9 English literatures. Meta-analysis results showed that: The overall incidence of COPD combined with anxiety or depression was 50.00%, the overall incidence of COPD combined with anxiety was 40%, the incidence of COPD combined with depression was 42%, and the incidence of COPD combined with anxiety and depression was 20%.

Conclusion: The incidence of COPD combined with anxiety and depression is high. Clinicians and patients' families should pay attention to COPD, and the psychological problems of patients, and prevent the occurrence of anxiety and depression.

Keywords: COPD, anxiety and depression, Meta-analysis

1. Introduction

Chronic obstructive pulmonary disease (COPD) is one of the third leading causes of death worldwide, after ischemic heart disease and stroke. COPD is a common, preventable and treatable disease characterized by persistent respiratory symptoms and airflow limitation due to airway and/or alveolar abnormalities, usually due to high exposure to harmful gases or particles.[¹] In the past three years, people's lives have been greatly affected by the novel coronavirus pneumonia.[²] The life of patients with COPD has also been greatly affected by COVID-19, such as: unable to go to the hospital regularly to review the condition, reduced communication with friends, reduced outdoor activities and so on. These factors are not conducive to the recovery of patients, and may even aggravate the condition, thus causing a great burden to society, life and medical treatment.[³] Studies have shown that COPD patients have more comorbidities, including dyspnea, cough/sputum production, sleep disorders, anxiety and depression, fatigue and pain, osteoporosis, etc., which increases the difficulty of its management.[⁴, ⁵] People usually pay attention to the physical damage of COPD patients, but relatively less attention to the comorbidities, especially the psychological problems.[⁶] At the same time, the body may increase anxiety and depression, the two interact, forming a vicious circle.[⁷] Therefore, the mental health of COPD patients is worthy of attention. COPD combined with anxiety and depression has been reported in different countries and regions, but it is different. In a retrospective study in the United Kingdom, anxiety and depression were common among patients with COPD, with rates of depression varying widely between 8% and 80% and rates of anxiety between 6% and 74%.[⁸] A study of hospitalized patients with COPD in Malaysia reported that 34.57% had anxiety and 38.27% had depression. 25.93% of the patients had both anxiety and depression.[⁹] However, to date, there has been no systematic review of the incidence of anxiety and depression in COPD patients to comprehensively analyze the reported incidence of anxiety and depression worldwide. Therefore, this study intends to conduct a systematic retrospective meta-analysis of the published incidence of anxiety and depression in COPD patients. To provide evidence-based medical evidence for clinical workers to further study COPD patients with anxiety and depression.
2. Data and Methods

2.1 Literature Search

Computer system search Web of Science, Cochrane Library, PubMed, Embase, Web of China National Knowledge Infrastructure (CNKI), China Biomedical Literature Service System, Wanfang Database, and VIP Database. The search time was from January 2018 to June 2022. The search was conducted by combining subject words and free words. Pulmonary Disease, Chronic Obstructive, Chronic Obstructive Lung Disease; D anxious, Depressive Symptoms. Chronic obstructive pulmonary disease (COPD), Anxiety, depression, psychological.

2.2 Literature Inclusion Criteria

(1) The subjects were patients with clinically confirmed COPD; (2) The study type was a cross-sectional study or another type of study that included baseline data. (3) Outcome indicators included the incidence of anxiety or depression; (4) The occurrence of anxiety or depression was assessed using standard scales, such as Generalized Anxiety Disorder-7 (GAD-7), Geriatric Depression Scale (GDS-15), Hospital Anxiety Depression Scale (HADS), Self-Rating Depression Scale (SDS), Self-Rating Anxiety Scale (SAS), Hamilton Anxiety Scale, Hamilton Depression Scale, (HAMD), (5) published and available full-text information, (6) language in Chinese or English (7) same author, Only studies with the most complete information were included if the same data were repeatedly published. (8) Excluded were case reports, review categories, unavailable full text, low literature quality [Agency for Healthcare Research and Quality (AHRQ) recommended cross-sectional Study Evaluation Scale score ≤3], and unable to contact the authors for complete data.

2.3 Literature Quality Evaluation

The cross-sectional study evaluation scale recommended by AHRQ was used to evaluate the quality of the included literature. The scale has 11 items, and the score ranges from 0 to 11 points: 0 to 3 is low quality, 4 to 7 is medium quality, and 8 to 11 is high quality. Two researchers searched and screened the literature respectively, compared the evaluation results, and reached an agreement on the controversial parts through discussion.

Table 1. Basic characteristics of included literature,

| Author       | Method          | Sample size | Average age | Sex ratio (M/W) | DC | AHRQ | Outcome indicator |
|--------------|-----------------|-------------|-------------|-----------------|----|------|------------------|
| Yi Xueyuan   | cluster sample  | 128         | 68.3±11.18  | 82/66           | HADS 8 | 1, 2 |
| Dai Jiangui  | cluster sample  | 200         | 65.7±11.3   | 104/96          | SADS 7 | 1, 2, 3, 4 |
| Liu Heping   | Questionnaire   | 312         | 68.7±13.5   | 227/89          | HADS 8 | 1, 2, 3 |
| Liu Ming     | cluster sample  | 68          | 67.3±13.2   | 30/88           | SADS 8 | 1, 2, 3 |
| Yu Yan       | cross-sectional | 120         | 75.1±5.6    | 78/42           | HAMA/BDI 7 | 1, 2, 3 |
| Liu Rong     | Questionnaire   | 438         | 75.5±7.8    | 234/204         | GDS-15 8 | 2    |
| Ji Juan      | Questionnaire   | 240         | 68.5±7.8    | 100/90          | SDS 8 | 2    |
| Zhang Xiaoyu | Questionnaire   | 229         | 67.4±11.2   | 47/43           | HADS 8 | 1, 2, 3, 4 |
| Zhu Jinhao   | Retrospective  | 109         | 69.5±13.4   | 72/77           | HADS 8 | 1, 2 |
| Li Zhenyuan  | Questionnaire   | 124         | 63.3±12.2   | 84/40           | SDS 8 | 2    |
| Li Xi        | Questionnaire   | 218         | 70.5±6.6    | 185/32          | SADS/SDS 8 | 1, 2, 3 |
| Liu Qing     | Questionnaire   | 145         | 65.4±10.6   | 113/32          | HADS 8 | 1, 2 |
| Geng Yi      | Questionnaire   | 84          | 68.5±12.2   | 48/36           | SAS 8 | 1    |
| Ke Cailia    | Questionnaire   | 111         | 62.1±13.2   | 89/22           | SDS 8 | 1, 2 |
| Mao Yongyu   | Questionnaire   | 180         | 65.3±11.7   | 102/78          | SADS/SDS 8 | 1, 2 |
| Wang Xiaohong| cluster sample  | 261         | 68.6±11.6   | 149/112         | SDS 8 | 2    |
| Wang Yuchao  | Cluster sample  | 286         | 68.6±11.6   | 202/85          | SADS/SRS 8 | 1, 2 |
| Tian Juan    | Cross-sectional | 236         | 74.6±10.8   | 106/130         | SADS/SRS 8 | 1, 2 |
| Chen Li      | Questionnaire   | 510         | 68.2±4.2    | 219/291         | GDS 8 | 2    |
| Huan Jiang   | Questionnaire   | 300         | 67.2±18.2   | 187/34          | SDS 8 | 2    |
| Luo Honghui  | Questionnaire   | 192         | 59.1±9.2    | 102/90          | SDS 8 | 1, 2 |
| Xiao Renshen | Questionnaire   | 141         | 65.3±7.9    | 117/24          | SDS 8 | 2, 3 |
| Chen Guosheng| Questionnaire   | 99          | 65.6±6.5    | 53/36           | SDS 8 | 1, 2, 3 |
| Qiu Yueting  | Questionnaire   | 196         | 64.3±7.9    | 100/96          | HAMD 8 | 2    |
| Chen Yan     | Questionnaire   | 100         | 73.8±11.3   | 59/41           | SDS 8 | 2    |
| Qi Guohua    | Questionnaire   | 154         | 69.3±11.5   | 94/60           | SDS 8 | 3    |
| Akiara       | Cross-sectional | 81          | 71.4±10.2   | 29/64           | GDS-15/GAD-7 8 | 1, 2, 3 |
| Barnes-Uldor | Cross-sectional | 293         | 68.2±10.3   | 229/64          | GAD 8 | 2    |
| S. K. Adhikari| Questionnaire   | 300         | 57.8±6.47   | 294/66          | HADS 8 | 1, 2 |
| E. H. Hasab  | Questionnaire   | 110         | 86.4±12.4   | 90/20           | HADS 8 | 2    |
| M. O. Hasam  | Questionnaire   | 293         | 67.1±10.3   | 200/93          | GAD 8 | 1, 2 |
| O. K. Vindu   | Questionnaire   | 80          | 76.9±7.3    | 60/20           | GAD 8 | 1, 2 |
| O. Kapliz     | Questionnaire   | 90          | 67.6±10.5   | 60/98           | GAD 8 | 1, 2 |
| S. Taminwala  | Cluster sample  | 100         | 67.1±11.5   | 97/13           | GAD 8 | 1, 2 |
| A. Wicciano   | Cohort study    | 51          | 66.8±7.0    | 42/91           | HADS 8 | 1, 2 |

Note: 1. Incidence of anxiety; 2. Incidence of depression; 3. Incidence of anxiety or depression; 4. Incidence of anxiety and depression.
2.4 Literature Screening and Data Extraction

All the literature was imported into EndNote20 software, and the primary screening was conducted by two researchers according to the title and abstract. After the primary screening, the kinds of literature were screened again after reading the full text. A total of 812 relevant literatures were initially screened. After reading the title, abstract, content and quality evaluation of relevant literatures, 775 literatures were excluded and 35 literatures. The data extracted included the first author and publication year, mean age, total sample size, male and female sample size, diagnostic criteria, number of occurrences of anxiety, number of occurrences of depression, number of occurrences of anxiety and depression, and survey instruments - Table 1 shows

2.5 Results of Meta-Analysis

2.5.1 Combined Anxiety Rate of COPD Patients

The combined results showed that the incidence of anxiety in COPD patients was 32%-48%, and there was great heterogeneity among the studies ($I^2 = 96.74%>50\%$, and $P<0.1$ for the Q test). Therefore, the random effect model was used for meta-analysis. The combined result was 40% [95%CI (32%,48%)], as shown in Figure 1.

![Figure 1. Meta-analysis on the anxiety rate](image)

Sensitivity analysis

Sensitivity analysis was carried out on the 25 literatures. After removing ZhangXiaoyu and Tianjuan data with large deviation, a Metaanalysis was conducted again on the retained data. Sensitivity analysis based on the random effect model showed that $I^2$ value was 94.84%. The overall incidence of anxiety in COPD patients was 43%[95%CI(36.0%,50%)], which was not significantly different from the heterogeneity and total incidence before the exclusion, indicating that the study results were robust, See the figure 2.
Subgroup analysis was conducted according to the different assessment scales of anxiety and depression, and the subgroup analysis was shown in Figure 3. See the subgroup analysis. The incidence of criterion 1 was 55%, criterion 2 was 24%, criterion 3 was 34%, and diagnosis 4 was 30%, where 1 indicated SAS/SDS, 2 indicated HAMA/HAMD, 3 indicated HADS, and 4 indicated.
Publication bias The funnel plot and Egger test were used to test the asymmetry of the literature, and the funnel plot showed incomplete symmetry, so the Egger test was used to test the publication bias of the literature, and the analysis results showed that $t=3.06$, $P=0.02$, $P$ less than 0.5. Preliminary judgment of publication bias is not obvious. See the Figure 4.

2.5.2 Incidence of Depression in COPD Patients

Analysis of the collected data showed that there was great heterogeneity ($I^2=96.74\%>50\%$, and $P<0.1$ of the $Q$ test). Therefore, the random effects model was used for meta-analysis, and the combined result was 42% [95%CI(36%,48%)] as shown in figure 5.

| Study          | ES (95% CI) | % Weight (Random) |
|----------------|-------------|-------------------|
| Y. Xueyan      | 0.37 (0.28, 0.46) | 3.11              |
| Dai Jiangni    | 0.38 (0.31, 0.45) | 3.17              |
| Liu Hongyi     | 0.37 (0.32, 0.43) | 3.21              |
| Liu Ming       | 0.54 (0.42, 0.67) | 2.96              |
| Liu Rong       | 0.35 (0.31, 0.40) | 3.24              |
| Ji Juan        | 0.33 (0.27, 0.40) | 3.19              |
| Zhang Xiaoyu   | 0.04 (0.02, 0.06) | 3.18              |
| Zhu Jinchao    | 0.48 (0.38, 0.57) | 3.07              |
| Li Zhenyi      | 0.23 (0.18, 0.31) | 3.10              |
| Li Xi          | 0.41 (0.34, 0.48) | 3.16              |
| Liu Qing       | 0.43 (0.35, 0.51) | 3.13              |
| Ke Calka       | 0.72 (0.63, 0.80) | 3.08              |
| Mao Yongju     | 0.69 (0.62, 0.76) | 3.16              |
| Wang Xiaohong  | 0.43 (0.36, 0.49) | 3.20              |
| Wang Yuchao    | 0.48 (0.42, 0.54) | 3.21              |
| Tian Juan      | 0.74 (0.68, 0.80) | 3.19              |
| Chen Li        | 0.57 (0.53, 0.61) | 3.24              |
| Huan Jiang     | 0.11 (0.07, 0.15) | 3.21              |
| Luo Honghui    | 0.40 (0.33, 0.47) | 3.17              |
| Xiao Renhui    | 0.27 (0.20, 0.35) | 3.12              |
| Chen Guosheng  | 0.48 (0.38, 0.59) | 3.03              |
| Guo Yongli     | 0.36 (0.29, 0.43) | 3.17              |
| Chen Yan       | 0.24 (0.16, 0.34) | 3.06              |
| Aqaidi         | 0.38 (0.28, 0.50) | 3.01              |
| Barreiro-Otero | 0.50 (0.44, 0.56) | 3.21              |
| S. K. Khalidi   | 0.26 (0.21, 0.31) | 3.21              |
| E. G. Heba     | 0.55 (0.46, 0.64) | 3.08              |
| M. O. Husain    | 0.51 (0.45, 0.57) | 3.21              |
| Ijames Atuku    | 0.40 (0.29, 0.52) | 3.03              |
| O. Kaplai       | 0.57 (0.46, 0.67) | 3.03              |
| S. Tammineedi   | 0.50 (0.40, 0.60) | 3.06              |
| A. Wozniczko    | 0.55 (0.40, 0.69) | 2.86              |
| Random Overall  | 0.42 (0.36, 0.48) | 100.00             |
| Fixed Overall   | 0.41 (0.40, 0.42) |                    |

Subgroup analysis
Due to the large heterogeneity of the data, the reasons were searched, and subgroup analysis was performed. The incidence of depression was 48% in diagnostic criterion 1, 54% in diagnostic criterion 2, 37% in diagnostic criterion 3, 45% in diagnostic criterion 4, and the overall incidence of post-merger depression was 42%. The specific situation is shown in Figure 6.

Bias test

Funnel plots showed incomplete symmetry, so the Egger test was used. The analysis results showed that t=4.08, P<0.00, and P less than 0.5 indicated no bias.

2.5.3 Incidence of Depression and Anxiety in Patients with COPD

The combined effect size and data analysis of anxiety and depression showed great heterogeneity ($I^2=95.14\%>50\%$, and $P<0.1$ of the Q test). Therefore, the random effect model was used for meta-analysis, and the combined result was 20% [95%CI(12%,31%)], as shown in figure 6.
Sensitivity Analysis

When drawing the star map, Huan Jiang, the bias of one paper was large, so it was removed to draw the forest map again. The combined results were I² = 64.84% > 50%, and the Q test P = 0.01 was less than 0.1. The heterogeneity was large, and the effect size was pooled by random effect. The combined result was 24% [95% CI (20%, 29%)].

Subgroup analysis According to different diagnostic criteria the included data were divided into 1-4 and 4 subgroups,
2.5.4 Rate of Anxiety or Depression in COPD Patients

Data analysis of anxiety or depression in COPD patients showed great heterogeneity ($I^2 = 94.35\% > 50\%$, and $P < 0.1$ for the Q test). Therefore, the random effects model was used for meta-analysis, and the combined result was 45\% [95\%CI (33\%, 58\%)], as shown in figure 6.

![Figure 6. Incidence of depression and anxiety.](image)

Sensitivity analysis

According to the forest map, Huan Jiang had a large bias on one paper, so it was removed to draw the forest map again. The combined result was $I^2 = 75.87\% > 50\%$, and the Q test $P = 0.000$ was less than 0.1. The heterogeneity was large, and the effect size was pooled by random effect. The combined result was 50\% [95\%CI(43\%, 57\%)].

Subgroup analysis

According to different diagnostic criteria, the included literatures were divided into 1-4 subgroups, and the results of each subgroup were relatively stable. The analysis results are shown in figure 7.

![Figure 7.](image)

Figure 7. 1 indicated SAS/SDS, 2 indicated HAMA/HAMD, 3 indicated HADS, and 4 indicated.
3. Discussion

The causes of anxiety and depression in patients with COPD are still unclear, and the research on them is in the initial stage. At present, the most widely accepted one is that COPD combined with anxiety and depression is the result of the joint action of many factors,

The most important of these factors is the damage caused by the disease itself, followed by smoking, having a spouse, unemployment, gender inequality, political instability, natural disasters, family discord, social pressure, lack of outdoor exercise, etc.

At the same time, a growing number of studies now prove that COPD is a psychosomatic disorder. Long-term pain, comorbidity, society, family, economy, and pressure lead to COPD patients not only suffering from the pain of the disease but also suffering from psychological suffering.

The results of this study showed that the incidence of COPD combined with anxiety was 40%, the incidence of depression was 42%, the incidence of anxiety or depression was 50.00%, and the incidence of COPD combined with anxiety and depression was 20%. This is in line with a previous review published in France, where the prevalence of anxiety and depression in COPD ranged from 6.7 to 58% and 5.5 to 51.5%, respectively.

In addition, Meta-analysis by Zhang et al. showed that among patients with stable COPD, 10-42% of patients were prone to depression and 10-19% to anxiety. In patients with an acute exacerbation of COPD, the risk of depression was significantly increased, even as high as 62%

It is slightly different from this study, and the reason may be that the patients included in this study were both in stable stage and acute exacerbation stage. At present, the majority of COPD patients with anxiety and depression have the problems of insufficient diagnosis, inadequate treatment, and even neglect of management. Insufficient diagnosis and neglect of management may lead to the error between the reported incidence of COPD complicated with anxiety and depression and the truth. Other studies have found that women with stable COPD have a higher risk of anxiety and depression than men.

Therefore, dyspnea in COPD patients is closely related to anxiety and depression. In addition, family environment is also associated with anxiety and depression in patients with COPD. A good family environment is conducive to physical and mental health, and family support can reduce the incidence of crisis in patients. Smoking is an important cause of COPD. Because smoking can cause neurological damage to the brain and decline in cognitive function. Moreover, chronic smokers with COPD have extensive cortical and subcortical structural dysfunction. Thus lead to the patient's emotional, psychological and other abnormalities.

Short-term studies have shown that both internal and external stress in COPD patients may lead to anxiety and depression. Internal pressure is dyspnea, wheezing, coughing, expectoration, external pressure, work, comments from friends, inability to do certain kinds of work due to lack of physical strength, etc. These causes contribute to the increase of anxiety and depression in COPD from different angles.

In the subgroup analysis, it can be seen that the assessment scale is different, and the results of each subgroup differ greatly. The reason may be the difference in the incidence of COPD complicated with anxiety and depression in different regions, or the difference in the assessment scale directly leads to the difference in the diagnosis results of COPD patients complicated with anxiety and depression. Therefore, it is suggested that all patients with possible COPD combined with anxiety and depression based on different scales should be further evaluated by psychiatrists to determine the diagnosis, which is conducive to the accuracy of disease diagnosis. The incidence of COPD combined with anxiety and depression is the result of multi-factors and multi-dimensions. The prevalence of COPD combined with anxiety and depression is high. Medical staff and patients' family members should actively pay attention to patients' mental health, and provide help for patients' rehabilitation by reducing the occurrence of anxiety and depression.

4. Conclusion

The overall incidence of COPD combined with anxiety or depression was 50.00%, the overall incidence of COPD combined with anxiety was 40%, the incidence of COPD combined with depression was 42%, and the incidence of COPD combined with anxiety and depression was 20%.

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