Original Article

Factors affecting the length of stay and hospital readmission rates after an acute exacerbation of chronic obstructive pulmonary disease: a systematic review and meta-analysis

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Background: Patients with chronic obstructive pulmonary disease (COPD) are often readmitted to hospital for treatment due to an acute exacerbation of the disease. However, there are few up-to-date studies investigating the lengths of stay and risk factors for readmission after an acute exacerbation of COPD. This study evaluated the length of stay in patients with an acute exacerbation of COPD and the factors that influenced their readmission.

Methods: A search of the PubMed, Cochrane Central Register of Controlled Trials, Embase, Web of Science, China National Knowledge Infrastructure (CNKI), Wanfang, and Weipu databases, carried out using the following search terms: airflow limitation, airway disease, airway obstruction, chronic obstructive pulmonary disease, COPD, length of stay and influencing factors, long-term oxygen therapy, lung disease, readmission, and respiratory system disease. The Cochrane risk of bias tool was used to evaluate the quality of the retrieved studies, and a network meta-analysis was performed using RevMan 5.20.

Results: Collectively, they included information on the length of stay for 630 patients who had been readmitted to hospital after an acute exacerbation of COPD (the readmitted group) and information on 688 patients who had not been readmitted (the non-readmitted group). Meta-analysis results showed that there was no difference in patient anxiety [risk ratio (RR) 1.22, 95% confidence interval (CI): 0.70–2.14] or long-term oxygen therapy (RR 1.91, 95% CI: 0.98–3.73) between the readmitted group and the non-readmitted group. However, there was a significant difference between the forced expiratory volume in one second (FEV1) predicted value [mean difference (MD) –5.85, 95% CI: –11.14 to –0.57] and the global initiative for chronic obstructive lung disease (GOLD) classification (C or D) (RR 1.61, 95% CI: 1.05–2.47).

Discussion: In summary, no significant relationship was found between patient state of anxiety, long-term oxygen therapy, length of hospital stay, and readmission rate after an acute exacerbation of COPD. However, FEV1 predicted values and GOLD classifications (C or D) had an impact on the length of hospital stay and readmission rate after acute exacerbation of COPD. Larger samples, multiple centers, and further research are needed to confirm the findings of this research.

Keywords: Chronic obstructive pulmonary disease (COPD); readmission; acute exacerbation; meta-analysis

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Introduction

Chronic obstructive pulmonary disease (COPD) is a lung disease characterized by progressive airflow limitation and decreased lung function. The clinical manifestations are a chronic cough, sputum expectoration, and dyspnea. In some patients, especially those with an acute exacerbation of COPD, wheezing may occur. The prevalence and fatality rate of COPD are on the rise, and it has become the third leading cause of death worldwide (1). The disease's slow, lengthy progress and chronic nature also create a significant economic and social burden (2). An acute exacerbation of COPD is defined as a sustained worsening in the patient's respiratory symptoms and usually requires adjustments to the patient's treatment plan (3). Acute exacerbations of COPD are associated with increased mortality, with in-hospital mortality ranging from 3% to 9% (4). In addition, an acute exacerbation of COPD will increase the number of doctor's visits required, the rate of hospital readmission, and the length of hospital stay, creating a significant burden on medical resources (5).

Furthermore, acute exacerbations of COPD, such as asthma, can reduce a patient's quality of life and significantly impact their work, leading to increased financial pressure and emotional anxiety (6). More seriously, an acute exacerbation of COPD may lead to loss of lung function, impaired health, comorbidity, and mortality (7-9). The causes of death of COPD include respiratory failure and cardiovascular disease caused by it, and influencing factors of survival time include ischemic heart disease, severe pulmonary hypertension, advanced age, body mass index, blood sugar and lung infections. The number of acute exacerbations per patient per year ranges from 1.2 to 2.4. Such a high frequency of acute exacerbations may have corresponding influencing factors, and as the severity of the disease increases, the frequency of acute exacerbations will also increase (10,11). The prevention or improvement of acute exacerbations has become the main goal of COPD treatment.

As hospitals implement measures to shorten the length of stay and reduce readmissions for patients with COPD, it is essential (especially from a socioeconomic standpoint) to quantify the length of stay after an acute exacerbation and identify the factors that lead to readmission. To date, few studies have evaluated the factors related to the duration of hospitalization and patient readmission after an acute exacerbation of COPD. Therefore, this study aimed to determine the duration of hospitalization and identify the factors that influence patient readmission after an acute exacerbation of COPD to provide relevant data that may contribute to the clinical prevention or improvement of acute exacerbations of COPD. We present the following article in accordance with the MOOSE reporting checklist (available at https://atm.amegroups.com/article/view/10.21037/atm-22-150/rc).

Methods

Search strategy

A search of the PubMed, Cochrane Central Register of Controlled Trials, Embase, Web of Science, China National Knowledge Infrastructure (CNKI), Wanfang, and Weipu databases from establishment to September 2021 was carried out using different combinations of the following search terms: airflow limitation, airway disease, airway obstruction, chronic obstructive pulmonary disease, COPD, length of stay and influencing factors, long-term oxygen therapy, lung disease, readmission, and respiratory system disease.

Inclusion and exclusion criteria

The inclusion criteria were as follows: (I) patients in the study cohort met the global initiative for chronic obstructive lung disease (GOLD) 2015 COPD diagnostic criteria; (II) patients in the study cohort were over 18 years old; (III) patients in the study cohort were divided into two groups (hospitalized and non-hospitalized) after an acute exacerbation of COPD; (IV) the study involved one or more research indicators of patient anxiety, long-term oxygen therapy, forced expiratory volume in one second (FEV1) predicted value, and GOLD classification (C or D); (V) the study compared the related factors of length of hospital stay and readmission rates for both readmitted and non-readmitted patients.

The exclusion criteria were as follows: (I) patients in the study cohort presented with stable COPD; (II) the study did not include research indicators in its inclusion criteria; (III) Reviews and case reports.

For multiple articles published by the same author, only the latest published data was selected.

Paper screening and risk of bias

Two qualified reviewers independently evaluated the title and abstract of the retrieved articles to determine whether

they met the inclusion criteria. If either reviewer found that the article met the criteria, the full text was reviewed. Disputes about the eligibility of an article were resolved by discussion with a third reviewer called in if consensus could not be reached. The Cochrane risk of bias tool was used to evaluate the quality of the selected articles and any risk of bias. The following characteristics were assessed: random sequence generation, allocation concealment, blinding of researchers and participants, blinding of outcome assessment, completeness of outcome data, selective outcome reports, and other biases. According to the evaluation, the biases were classified into high-risk, low-risk, and unclear.

Data extraction

The patients from the selected studies were divided into two groups: (I) those who had been readmitted to hospital after an acute exacerbation of COPD and for whom length of stay data was available (the readmitted group); and (II) those who had not been readmitted to hospital, for whom there was no length of stay data (the non-readmitted group). The two reviewers independently extracted the following data, as required for the present study: study author(s), country, publication date, journal name, and patient demographic. Outcome indicators for patient anxiety, long-term oxygen therapy, FEV1 predicted values, and GOLD classifications (C or D) were also recorded.

Statistical analysis

An I^2 test was used to test for heterogeneity. If the heterogeneity between studies was not significant (P>0.1, I^2<50%), the fixed-effects model was used to merge the effect sizes. If the heterogeneity between studies was significant (P≤0.1, I^2≥50%), the random-effects model w used to merge the effect size. Percentages and relative risk (RR) or mean difference (MD) with a 95% confidence interval (CI) were used to describe the data. Statistical analyses were performed using the RevMan 5.20 software provided by the Cochrane Collaboration (UK). A P value of less than 0.05 was considered statistically significant. A funnel plot was used to check the risk of publication bias.

Results

Search results and study characteristics

A total of 570 records were retrieved from the databases. Of these, 68 were eliminated after the initial screening, and 63 were excluded due to their low quality. Of the 439 remaining articles, 148 were cannot be retrieved. A total of 291 articles were retrieved, all articles were read in full. After applying the inclusion and exclusion criteria, eliminating reviews, case reports, and articles without study indicators. Seven articles were selected for inclusion. The selection process is shown in *Figure 1*.

Of the 7 selected articles, 4 reported on patients' state of anxiety, 4 reported on bleeding events, 3 reported on long-term oxygen therapy, 3 reported on the FEV1 predicted values, and 3 reported on the GOLD classifications (C or D). All selected articles included clear diagnoses and inclusion and exclusion criteria. Collectively, the studies included 1,318 patients, of whom 630 were categorized into the readmitted group and 688 into the non-readmitted group. The basic characteristics of the articles are shown in *Table 1*.

None of the selected articles described the risk of bias assessment for random sequence generation, allocation hiding, blinding (of participants and researchers), or blinding of outcome assessment. All articles described the risk for complete outcome data bias, selective reporting bias, and other risks of bias. The assessment results are shown in *Figure 2*.

Meta-analysis results

State of anxiety

A total of 4 articles analyzed the difference in anxiety levels between readmitted and non-readmitted patients after an acute exacerbation of COPD. Collectively, these articles included 441 patients with COPD who were readmitted to hospital and 497 who were not. Analysis of these results showed (P=0.03, I^2=67%), indicating heterogeneity in anxiety levels between readmitted and non-readmitted patients after an acute exacerbation of COPD. Therefore, a random-effects model was used for the combined analysis. The combined effect size RR was 1.22, 95% CI: (0.70–2.14) (*Figure 3*). The result of the combined effect size test was Z=0.70, P=0.49, which showed that differences in the state of anxiety between the readmitted and non-readmitted patients after an acute exacerbation of COPD were not statistically significant.

Long-term oxygen therapy

A total of 3 articles analyzed the differences in long-term oxygen therapy between patients who were readmitted to hospital after an acute exacerbation of COPD and those

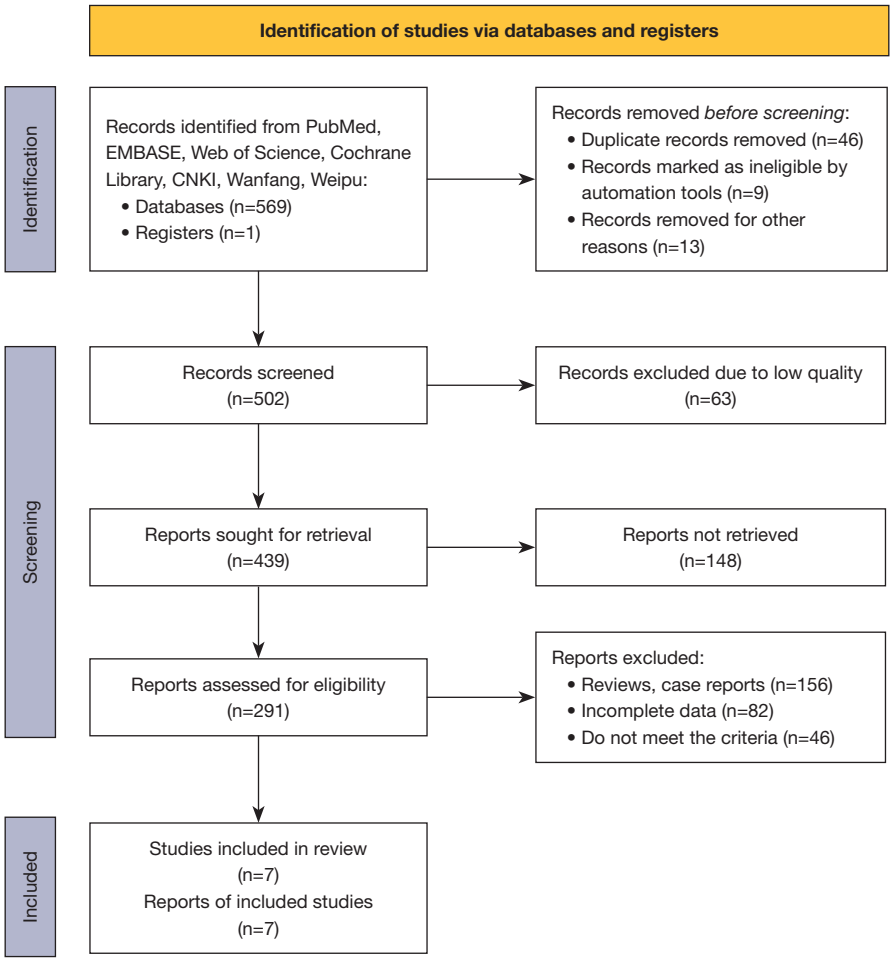

Figure 1 Flow diagram of the search, screening, and inclusion processes.

Table 1 Basic characteristics of the selected articles

Author	Country	Year	Journal	Readmitted (n)	Non-readmitted (n)
Tsui *et al.* (12)	China	2016	*Int J Tuberc Lung Dis*	44	165
Zhang *et al.* (13)	Singapore	2014	*Int J Respir*	66	71
Gudmundsson *et al.* (14)	Iceland	2005	*Eur Respir J*	246	160
Cao *et al.* (15)	China	2006	*Respirology*	85	101
Anbesse *et al.* (16)	Ethiopia	2020	*PLoS One*	71	71
Almagro *et al.* (17)	Spain	2006	*Respiration*	75	54
Wong *et al.* (18)	British Columbia	2008	*Can Respir J*	43	66

who were not. The total number of cases included 361 readmitted patients and 396 non-readmitted patients. The analysis results (P=0.02, I^2=74%) indicated that heterogeneity in the long-term oxygen therapy existed between readmitted and non-readmitted patients after an acute exacerbation of COPD. Therefore, the random-effects model was used for the combined analysis. The combined effect size RR was 1.91, 95% CI: (0.98–3.73)

(*Figure 4*). The result of the combined effect size test was Z=1.90, P=0.06, indicating that there was no statistical significance in the long-term oxygen therapy differences between readmitted and non-readmitted patients after an acute exacerbation of COPD.

FEV1 predicted value

A total of 3 articles analyzed the difference in FEV1 predicted values for patients who were readmitted to hospital after the acute exacerbation of COPD and those who were not. The total number of cases included 365 readmitted patients and 379 non-readmitted patients. The analysis results (P=0.010, I^2=78%) indicated heterogeneity in the FEV1 predicted values for readmitted and non-readmitted patients after an acute exacerbation of COPD. Therefore, the random-effects model was used for combined analysis. The combined effect size MD was −5.85, 95% CI: (−11.14 to −0.57) (*Figure 5*). The combined effect size test result was Z=2.17, P=0.03, indicating that the differences between FEV1 predicted values for readmitted and non-readmitted patients after an acute exacerbation of COPD were statistically significant.

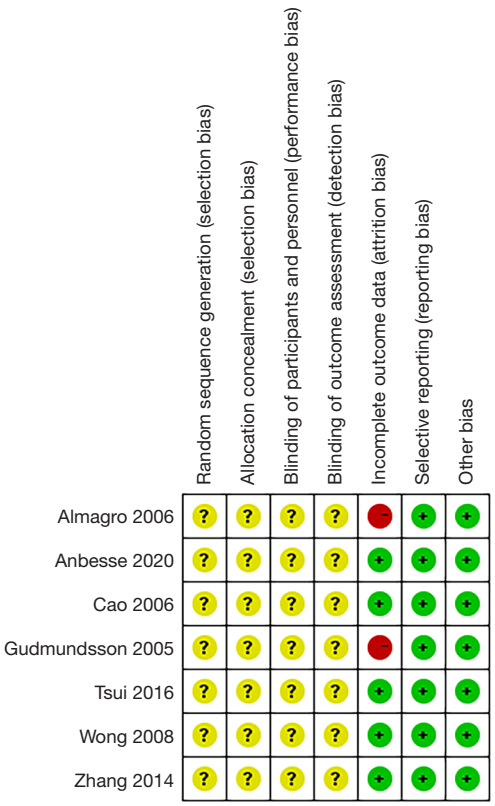

Figure 2 Article quality evaluation details.

GOLD classification (C or D)

A total of 3 articles analyzed the difference in GOLD classifications (C or D) between patients who were readmitted to hospital after an acute exacerbation of COPD and those who were not. The total number of cases included 172 readmitted patients and 332 non-readmitted patients. The analysis results (P=0.005, I^2=81%), indicated heterogeneity in GOLD classifications (C or D) between readmitted and non-readmitted patients after an acute exacerbation of COPD. Therefore, the random-effects model was used for combined analysis. The combined effect size RR was 1.61, 95% CI: (1.05–2.47) (*Figure 6*). The combined effect size test result was Z=2.20, P=0.03, indicating that the differences in GOLD classification (C or D) between readmitted and non-readmitted patients after an acute exacerbation of COPD were statistically significant.

Publication bias

Although the total number of articles included in the analysis was 7, the number of articles included for

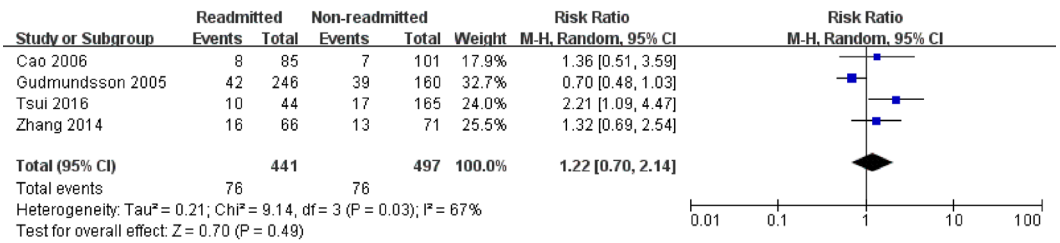

Figure 3 Forest plot of patient state of anxiety. Comparison of state of anxiety between the readmitted group and the non-readmitted group. Statistical method: Mantel-Haenszel random-effects model (RR and 95% CI). RR, relative risk; CI, confidence interval.

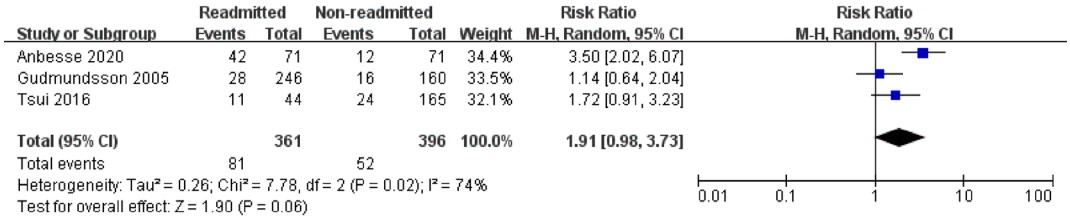

Figure 4 Forest plot of long-term oxygen therapy. Comparison of long-term oxygen therapy between the readmitted group and the non-readmitted group. Statistical method: Mantel-Haenszel random-effects model (RR and 95% CI). RR, relative risk; CI, confidence interval.

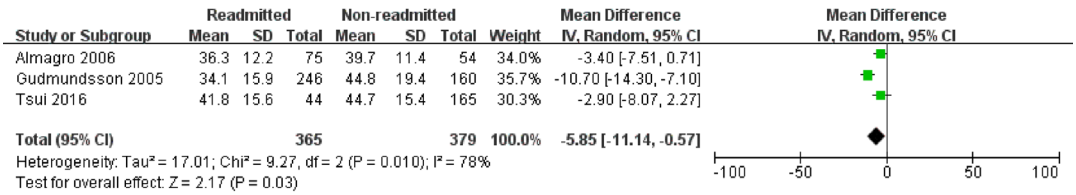

Figure 5 Forest plot of FEV1 predicted values. Comparison of FEV1 predicted values between the readmitted group and the non-readmitted group. Statistical method: inverse variance random-effects model (MD and 95% CI). FEV1, forced expiratory volume in one second; MD, mean difference; CI, confidence interval.

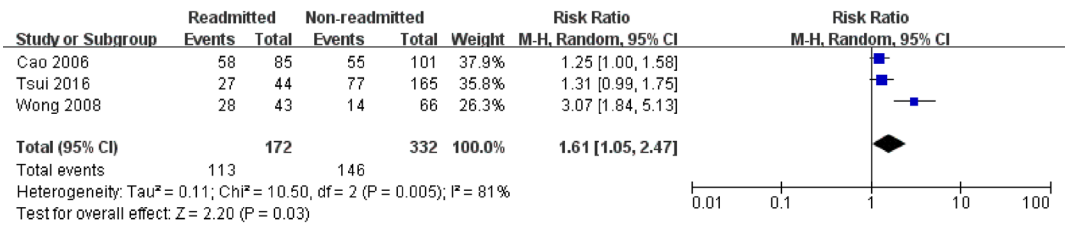

Figure 6 Forest plot of GOLD classifications (C or D). Comparison of GOLD classifications (C or D) between the readmitted group and the non-readmitted group. Statistical method: Mantel-Haenszel random-effects model (RR and 95% CI). GOLD, global initiative for chronic obstructive lung disease; RR, relative risk; CI, confidence interval.

each index was lower than 5, which did not reach the number required for publication bias analysis. Therefore, publication bias analysis was not performed.

Risk of bias

None of the selected articles described the risk of bias for random sequence generation, allocation concealment, blinding of participants and researchers, or blinding of outcome assessment, so the above biases were all considered low-risk. Two articles had a high risk of bias from incomplete result data (14,17), and 5 articles had a low risk of bias from incomplete result data (12,13,15,16,18). Selective reporting domains and other biases for all articles were low-risk (*Figure* 7).

Discussion

In the past few years, patients with COPD have received better treatment with more effective long-acting bronchodilators, but since the progress of drug therapy, there have been few up-to-date studies reviewing the risk factors for hospital readmission and length of stay after acute exacerbations of COPD. The GOLD guidelines were revised in 2011 and recommended a comprehensive assessment of COPD based on symptoms, vital capacity classification, and history of acute exacerbations. One or more hospitalizations for acute exacerbations of COPD

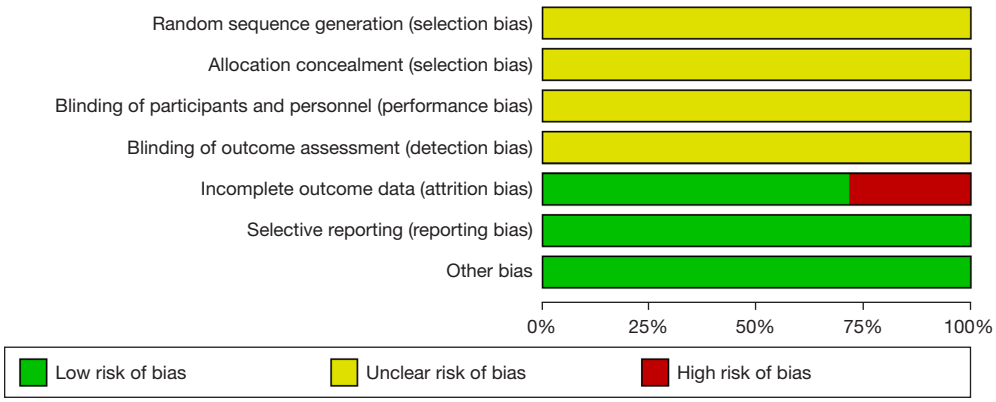

Figure 7 Intensity and distribution of risk of bias for the articles included in the study.

are considered high-risk, and the recommended treatment is inhaled corticosteroid (ICS) and a long-acting beta-agonist (LABA) and/or long-acting muscarinic antagonists (LAMAs) (19). All patients in this study were classified as high-risk patients (20). Studies have shown that although the treatment of COPD has improved in recent years, readmission rates after an acute exacerbation of COPD are still high, with 73.2% of patients being readmitted to hospital at least once within 1 year after discharge (12). In addition, a large proportion of patients with COPD are readmitted to hospital very frequently, with 21.1% of patients having been readmitted more than 4 times within a year for varying lengths of hospital stay (12).

Anxiety is a common comorbidity in patients with COPD, but it often remains undetected and untreated. A systematic review found that the prevalence of clinical anxiety is high, with the proportion of inpatients who present with the anxiety condition ranging from 10% to 55%, and the proportion of outpatients with anxiety ranging from 13% to 46% (21). Anxiety has a negative impact on the quality of life of patients with COPD and is related to more severe disability and impaired functional status (22). In an earlier study, anxiety was shown to be an important risk factor for the readmission of patients with COPD (14,23). However, our analysis found that anxiety was not significantly associated with readmission and length of stay for patients with COPD. In this study, long-term oxygen therapy was also found to have no strong correlation with hospital readmission and length of stay after an acute exacerbation of COPD. A possible reason for the lack of association between these factors and rehospitalization in the current study may be the study's small sample size.

Pulmonary function status (measured by FEV1) and GOLD classifications have also been shown to be significantly related to the risk of readmission to hospital after an acute exacerbation of COPD, and the length of stay in hospital during admission has been shown to be significantly longer than that of other patients with COPD (18). Our analysis found an association between FEV1 predicted values and readmission and length of stay for patients with COPD. It also found that the FEV1 predictive value can represent a risk factor for readmission and a longer hospital stay after an acute exacerbation of COPD. At the same time, other studies (15,23,24) have found that a FEV1 <50% can be a predictor of the risk of readmission after an acute exacerbation of COPD, which aligns with our research conclusions. Our research also confirmed that a GOLD classification of C or D is also a factor that influences readmission and length of hospital stay for patients after an acute exacerbation of COPD. The rehospitalization rate of patients in the acute exacerbation of COPD is as high as 60%, and the mortality rate of patients can be significantly reduced after hospitalization (14,17).

This study has certain limitations. First, because the relevant indicators included in the study are objective, there is a lack of randomized controlled studies. Second, the sample size for the present study was small and lacked representativeness. Third, the literature included few recently published articles. Therefore, further large-scale, multi-center studies are needed to confirm the factors affecting the readmission and length of stay for patients after an acute exacerbation of COPD. Despite these limitations, this study systematically evaluated the effects of anxiety, long-term oxygen therapy, FEV1 predicted values, and GOLD classifications on the rehospitalization and length of hospital stay on patients after an acute

exacerbation of COPD. In addition to the above factors, nutritional improvement can improve the immunity of the patient, and contribute to the improvement of short-term recovery and long-term prognosis. Future research should consider nutritional intervention.

Conclusions

We selected 7 articles concerning the factors affecting the length of stay and readmission rate of patients after acute exacerbations of COPD and analyzed and systematically reviewed patient anxiety, long-term oxygen therapy, FEV1 predicted values, and GOLD classifications. The results showed that the state of anxiety and long-term oxygen therapy had no significant relationship to the length of stay and readmission rate after an acute exacerbation of COPD, but that the FEV1 predicted value and GOLD classification (C or D) did have an effect on the length of stay and readmission rate after an acute exacerbation of COPD. However, further research with a larger sample and multiple center-based data is needed to confirm the findings of this research.

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Footnote

Reporting Checklist: The authors have completed the MOOSE reporting checklist. Available at https://atm.amegroups.com/article/view/10.21037/atm-22-150/rc

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://atm.amegroups.com/article/view/10.21037/atm-22-150/coif). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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