Postprint of a Scoping Review on Fatigue in Patients with Chronic Obstructive Pulmonary Disease

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Abstract

Background: Chronic Obstructive Pulmonary Disease (COPD) is a global public health problem with increasing incidence and mortality rates. Fatigue is one of the common complaints among COPD patients and significantly impairs their quality of life. Objective: To conduct a scoping review of the current status and influencing factors of fatigue in COPD patients, to provide insights for developing personalized interventions. Methods: Using the scoping review framework proposed by Arksey and O' Malley, research questions were established. Literature in Chinese and English from various databases was searched and screened from inception to July 2022 to identify relevant studies. Data extraction, collection, and synthesis were performed, and the findings were reported. Results: A total of 51 studies were included. The results showed that assessment tools for fatigue in COPD patients are diverse, but generally lack multidimensionality and specificity. The most commonly used tools in the studies were the Functional Assessment of Chronic Illness Therapy-Fatigue (FACIT-F) scale and the Fatigue Severity Scale (FSS). The incidence, duration, and severity of fatigue varied across different studies. The main influencing factors of fatigue included sociodemographic factors, disease-related factors, physical factors, and psychological factors. Conclusion: Fatigue is a significant symptom in COPD patients that severely affects quality of life. Clinical healthcare professionals should utilize specific assessment tools for accurate evaluation and develop personalized interventions based on influencing factors to improve fatigue symptoms.

Full Text

Preamble

Fatigue Study in Patients with Chronic Obstructive Pulmonary Disease: A Scoping Review

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Abstract

Background: Chronic obstructive pulmonary disease (COPD) is a global public health problem with increasing incidence and mortality rates. Fatigue is one of the most common complaints among COPD patients and has a serious negative impact on their quality of life. **Objective:** To conduct a scoping review of the current status and influencing factors of fatigue in COPD patients to provide insights for developing personalized intervention strategies. **Methods:** Using the scoping review framework proposed by Arksey and O' Malley, we established research questions and systematically searched and screened Chinese and English literature from various databases up to July 2022. Relevant studies were identified, and data were extracted, collected, summarized, and reported. **Results:** A total of 51 articles were included. The results showed that while various assessment tools exist for evaluating fatigue in COPD patients, most lack multidimensionality and specificity. The most commonly used instruments were the Functional Assessment of Chronic Illness Therapy (FACIT) and the Fatigue Severity Scale (FSS). The reported incidence, duration, and severity of fatigue varied across studies. Major influencing factors included sociodemographic factors, disease-related factors, physical factors, and psychological factors. **Conclusion:** Fatigue is a significant symptom that seriously affects quality of life in COPD patients. Healthcare professionals need to use specific assessment tools for accurate evaluation and develop personalized interventions based on identified influencing factors to improve fatigue symptoms.

Keywords: Chronic Obstructive Pulmonary Disease; Fatigue; Assessment Tools; Influencing Factors; Scoping Review

1.1 Research Questions

This study established research questions based on the PCC (Participant, Concept, Context) principle formulated by Peters et al. The participants were patients diagnosed with COPD. The concept was "fatigue," defined as a subjective, unpleasant symptom encompassing a whole-body sensation ranging from tiredness to exhaustion that interferes with normal life. The context referred to any environment where patients might be located, such as medical or healthcare institutions, nursing facilities, communities, or homes. After preliminary literature review and team discussion, the following questions were identified: (1)

What assessment tools can measure fatigue in COPD patients? (2) What is the current status of fatigue among COPD patients domestically and internationally? (3) What factors influence fatigue in COPD patients?

1.2 Inclusion and Exclusion Criteria

Inclusion criteria: (1) Chinese and English literature; (2) Study subjects were COPD patients, or included COPD patients with extractable complete data; (3) Literature explored the status and influencing factors of fatigue in COPD patients using clearly defined tools to measure subjective fatigue; (4) Primary literature with original data analysis was included. **Exclusion criteria:** (1) Interventional study designs; (2) Literature types including reviews, systematic reviews, qualitative studies, conference abstracts, and dissertations; (3) Literature where full text was unavailable; (4) Duplicate publications.

1.3 Literature Search

A combination of subject headings and free-text terms was used to search six English databases (Web of Science, PubMed, Embase, CINAHL, ProQuest, Cochrane Library) and four Chinese databases (CNKI, Wanfang, VIP, and Chinese Biomedical Database) from inception to July 2022. The PubMed search strategy, for example, was: ("pulmonary disease, chronic obstructive" [MeSH Terms] OR "chronic obstructive lung disease" [Title/Abstract] OR "chronic obstructive pulmonary diseases" [Title/Abstract] OR "COPD" [Title/Abstract] OR "COAD" [Title/Abstract] OR "chronic obstructive airway disease" [Title/Abstract] OR "chronic airflow obstruction*"[Title/Abstract]) AND ("fatigue" [MeSH Terms] OR "Exhaustion"[Title/Abstract] OR "Lassitude"[Title/Abstract] OR "Tiredness" [Title/Abstract] OR "energy loss" [Title/Abstract] OR "mental fatigue" [Title/Abstract]). The Chinese CNKI search strategy was: (SU= '慢性阻塞性肺疾病' + '慢阻肺' + 'COPD') AND (SU= '疲劳' + '疲乏). Additionally, references of included studies were manually traced to improve comprehensiveness.

1.4 Literature Screening

A research team was formed with all members receiving standardized evidence-based nursing training. After importing literature into NoteExpress 3.5 for organization and deduplication, screening proceeded in three steps. First, two members randomly selected 30 articles to practice title and abstract screening to reach consensus on data extraction principles. Then, two members independently reviewed titles and abstracts of all literature according to inclusion criteria for initial screening. Finally, full texts were carefully read and evaluated against exclusion criteria for secondary screening. Any disagreements were resolved by consulting a third team member to reach consensus.

1.5 Data Extraction and Analysis

NoteExpress 3.5 and Microsoft Excel were used for cataloging and sorting data. Two team members independently extracted data from each article, with disagreements discussed with a third member. Extracted data were summarized and entered into Excel spreadsheets. The extracted information included: (1) Basic characteristics: country, author, publication year, study type; (2) Key content: assessment tools, current status (incidence/level) of fatigue, and influencing factors; (3) Survey information: sample size and data source.

2.1 Literature Search Results

A total of 12,113 articles were retrieved: 440 from PubMed, 2,487 from Web of Science, 2,119 from Embase, 1,903 from CINAHL, 2,025 from ProQuest, 578 from Cochrane Library, 511 from CNKI, 844 from Wanfang, 559 from VIP, and 667 from the Chinese Biomedical Database. Additionally, 15 articles were identified through reference tracking, as many studies included fatigue as a secondary outcome not mentioned in titles or abstracts. After screening, 51 articles were ultimately included. The literature screening flowchart is shown in Figure 1 [Figure 1: see original paper].

2.2 Characteristics of Included Studies

The final inclusion consisted of 51 articles, including 46 in English and 5 in Chinese. Publication years ranged from 1998 to 2021, with a rapid increase in publications between 2010-2019. Studies were conducted across 16 countries on five continents: 23 studies in Europe (Sweden 7, Netherlands 4, UK 4, Norway 3, Spain 2, Greece 1, France 1, Romania 1), 10 in North America (USA 7, Canada 3), 1 in South America (Brazil), 1 in Oceania (Australia), and 17 in Asia (China 8, Turkey 7, Japan 1, South Korea 1). Sample sizes ranged from 19 to 2,696 participants. Cross-sectional studies dominated (n=41), including 14 comparative studies. Other designs included 4 cohort studies, 4 longitudinal studies, 1 case-control study, and 1 mixed-methods study. Regarding data sources, 30 studies were from single centers and 21 from multicenter settings. Detailed characteristics are summarized in Table 1 .

2.3 Assessment Tools for Fatigue in COPD Patients

Twenty-two different assessment tools were used across the included studies (detailed information in Table 2). In terms of measurement purpose, tools could be categorized as assessing either fatigue severity or fatigue impact. Regarding scoring, most tools indicated higher scores represented worse fatigue, except for the Chronic Respiratory Questionnaire (CRQ), 36-item Short-Form Health Survey (SF-36), and Functional Assessment of Chronic Illness Therapy (FACIT), where higher scores indicated less severe fatigue. Ten tools defined fatigue cutoff values, with only the Checklist Individual Strength (CIS) specifically distinguishing between normal fatigue and pathological fatigue. In terms of specificity, only

the Fatigue Impact Scale (FIS), Manchester COPD Fatigue Scale (MCFS), and COPD and Asthma Fatigue Scale (CAFS) were disease-specific. The most frequently used tool was FACIT (n=10), followed by the Fatigue Severity Scale (FSS) (n=9). These popular tools shared common features: fewer items for easy completion and defined cutoff values, making them suitable both as standalone screening tools and in combination with other scales to measure activity limitation caused by fatigue.

2.4 Current Status of Fatigue in COPD Patients

Among the 51 included articles, 21 reported fatigue incidence rates ranging from 36% to 88.26%. Four articles reported overall fatigue levels as moderate or moderate-to-high. Fourteen studies compared COPD patients with different control groups, with most finding fatigue more prevalent and severe in COPD patients. Specifically, seven studies indicated higher fatigue severity in COPD patients compared to healthy controls, three showed higher fatigue proportions, two demonstrated higher frequency and duration, one found higher fatigue proportions only in male participants, while one reported no significant difference in fatigue scores between COPD patients and healthy controls.

2.5.1 Sociodemographic Factors

Age, gender, education level, income, marital status, and smoking history may all influence fatigue in COPD patients. Some studies reported that older patients experienced higher fatigue levels compared to younger patients, while others observed the opposite pattern. Female COPD patients showed higher average fatigue levels and greater proportions of severe fatigue compared to males, though one study found no statistically significant gender difference. Patients with lower education and income levels were more prone to fatigue and had poorer energy levels. Patients with partners reported lower fatigue than those without, while married patients experienced more fatigue than single patients, and widowed patients reported more fatigue than married or unmarried individuals. Smoking was also a major risk factor, with more frequent smoking and longer smoking history associated with more severe fatigue.

2.5.2 Disease-Related Factors

Twenty-four studies extensively examined the relationship between dyspnea and fatigue, consistently showing moderate-to-high positive correlations between dyspnea severity and fatigue levels. Eighteen articles demonstrated that disease severity affected fatigue levels, primarily through airflow limitation from poor lung function, though the overall correlation was weak. Four studies explored associations between exacerbation frequency and fatigue, finding significantly higher fatigue levels in patients with more frequent exacerbations. Comorbidities such as heart disease, sleep apnea syndrome, restless legs syndrome, frailty, pain, and respiratory symptoms also increased fatigue severity. Two studies in-

vestigated relationships between inflammatory markers and fatigue, with CRP and TNF-α levels positively correlated with fatigue. Additionally, more frequent medication use, hospitalizations, and treatment sessions were associated with greater fatigue perception.

2.5.3 Physical Factors

Twenty studies identified physical activity level as a predictor of fatigue. Poorer self-care ability and more severe disability were associated with heavier fatigue, while better exercise endurance, longer exercise duration, and more frequent weekly exercise were associated with lighter fatigue. Five studies examined relationships between muscle strength and fatigue, finding strong negative correlations with grip strength, isometric muscle strength, quadriceps strength, abdominal muscle strength, and shoulder muscle strength. Three studies reported relationships between BMI and fatigue, with both high and low BMI increasing fatigue. Sleep quality was also closely linked to fatigue, with sleep disorders directly or indirectly exacerbating fatigue.

2.5.4 Psychological Factors

As a major stressor for COPD patients, fatigue leads to many negative emotions, with anxiety and depression being the most common psychological conditions. Nine studies reported relationships between anxiety and fatigue, while fourteen described associations between depression and fatigue, all indicating significant positive correlations. Additionally, kinesiophobia, loss of will, and self-perceived burden were positively correlated with higher fatigue levels. Patients' fatigue levels were also closely related to their illness perceptions, with self-perceived health control and future expectations negatively correlated with fatigue. Health locus of control, which describes patients' self-care abilities, was also positively correlated with fatigue, with externally-oriented patients showing less confidence and poorer disease control.

3.1 Analysis of Fatigue Assessment Tools for COPD Patients

Fatigue in COPD patients is a complex, multidimensional concept, sometimes termed COPD-related fatigue, representing a combination of physical, mental, and social states. However, previous research has focused primarily on physical fatigue, such as diaphragmatic muscle fatigue, while neglecting other dimensions. Consequently, most assessment tools were designed to measure physical fatigue and are predominantly unidimensional generic scales. COPD-related fatigue differs from fatigue in other diseases and requires multidimensional, disease-specific instruments validated through large-scale studies. When measuring fatigue prevalence, it' s important to consider that fatigue is also common in healthy populations. Therefore, future assessment tool development should

distinguish between normal and pathological fatigue through comparative validation between COPD patients and healthy subjects. While more items can improve accuracy, the most frequently used scales were shorter, offering easier administration and better completion rates, particularly during busy clinical periods. This convenience is an important consideration for researchers, suggesting that tool design should balance convenience and accuracy.

Analysis of domestic studies revealed that no universally recognized fatigue questionnaires were used in COPD fatigue research in China, with each study employing different translated versions. China has yet to develop a domestic COPD-specific fatigue measurement tool. The limited number of studies indicates an urgent need to develop more accurate, reasonable, and culturally appropriate assessment tools for Chinese COPD patients through comprehensive literature review and qualitative research.

3.2 Analysis of Fatigue Status in COPD Patients

Due to diverse measurement tools, different cutoff values and severity classifications, and cultural variations in scale dimensions/items across countries, reported fatigue incidence and severity vary considerably, making reliable comparisons difficult. Assessment tool usage also presents issues. For example, while FACIT was most frequently used, some scholars defined fatigue cutoff values as $ $43 points, whereas most studies did not describe cutoff criteria in detail before drawing conclusions about fatigue severity. In Yang' s study, a brief version was used with fatigue classified into mild, moderate, and severe levels. Similar inconsistencies appeared in studies using FSS, where most defined fatigue as mean item score $ $4, but Inal-Ince defined $ $4 as severe fatigue and <4 as mild fatigue, while Cavalcante used total score $ $27 as the cutoff. Researchers should standardize assessment tool usage, clarify cutoff criteria for COPD fatigue, and standardize reporting.

3.3.1 Sociodemographic Factors

Regarding demographic factors, findings on marital status, income level, and smoking habits were consistent, but age and gender relationships with fatigue remain controversial. Some studies reported higher fatigue in older patients, while others found higher fatigue in younger patients, possibly due to different assessment tools. Older patients' fatigue may be primarily physical, while younger patients' fatigue may be more psychosocial, reflecting the multidimensional nature of fatigue that existing tools fail to capture comprehensively. For gender, Goërtz, Miravitlles, and Kapella reported heavier fatigue in female patients, while Theander found no statistically significant gender differences. These inconsistencies may relate to gender distribution in samples, regional differences, and uncontrolled confounding factors. Some studies had small female sample sizes, leading to potential 偶然性, while different healthcare levels and cultural backgrounds across countries may influence results. More multicen-

ter, large-sample studies controlling for confounders are needed to explore these controversial demographic factors.

3.3.2 Disease-Related Factors

Previous studies suggested that lung function directly affects fatigue levels, but most included studies showed weak associations. One longitudinal study found that despite stable lung function over four years, the proportion of patients with severe fatigue doubled. This suggests lung function may not be a direct cause of fatigue but may influence it indirectly through dyspnea and other mechanisms. Many studies confirmed that dyspnea independently affects fatigue, being the primary influencing factor, particularly on physical function. Elevated inflammatory markers like CRP and TNF-α may also indirectly worsen fatigue by aggravating dyspnea. Comorbidities and disease exacerbations were identified as fatigue risk factors, possibly sharing pathological mechanisms with fatigue. Positive correlations between treatment frequency, medication quantity, and fatigue may relate to limited effects of pulmonary medications and their side effects. Longitudinal prospective studies are needed to explore underlying mechanisms between these disease factors and fatigue.

3.3.3 Physical Factors

Progressive exercise limitation is a hallmark of COPD. Physical activity level and peripheral muscle strength are protective factors against fatigue. Regular physical activity can alleviate muscle atrophy and help patients adapt to fatigue. Patients with lower muscle strength perceive physical fatigue more intensely because disease progression increases muscle metabolic consumption and alterations, reducing muscle strength and exacerbating fatigue perception. Nutritional status also affects fatigue: high BMI causes obstructive sleep apnea, disrupting sleep and causing daytime fatigue, while low BMI reduces immune function and respiratory muscle capacity, impairing ventilation and worsening fatigue. Sleep disorders, as serious circadian rhythm disturbances, impair normal recovery and increase fatigue susceptibility. Comprehensive assessment of physical function, early monitoring of physical activity, muscle strength, nutrition, and sleep indicators are needed to develop safe and effective interventions.

3.3.4 Psychological Factors

Patients develop different psychological responses when facing disease impacts. Positive attitudes, belief in self-control over health, and hope for the future promote health-related behaviors and outcomes that alleviate fatigue. Conversely, negative attitudes lead to anxiety, depression, kinesiophobia, self-perceived burden, and loss of will, increasing fatigue severity. Studies show that psychological factors often co-occur with disease-related and physical factors, interacting to influence fatigue. For example, almost all COPD patients with clinical depression and anxiety experienced fatigue and had poorer lung function and more severe

dyspnea. Dyspnea, anxiety, depression, and sleep 障碍相互影响, 共同作用于疲劳. Lee developed a structural equation model analyzing relationships among dyspnea, anxiety, depression, physical function, and fatigue, finding these variables could influence fatigue both directly and indirectly as mediators. Therefore, COPD fatigue causes are complex, and correlations between specific factors and fatigue only suggest shared underlying mechanisms, not causal relationships.

4 Limitations

First, only Chinese and English literature was included, potentially excluding relevant studies in other languages. Second, this review analyzed included literature without rigorous quality assessment. Third, conference abstracts were excluded, possibly missing latest research findings and limiting conclusion applicability. Fourth, this review focused only on assessment tools, status, and influencing factors, excluding all interventional studies, thus preventing accurate determination of fatigue mechanisms; future reviews could expand the scope. Fifth, literature categorization and data extraction inevitably involved some subjectivity, representing a potential limitation.

Summary and Outlook

This scoping review indicates that fatigue measurement tools need further refinement in design and usage, and inconsistent severity classifications prevent reliable conclusions about fatigue incidence and levels. The specific etiology and mechanisms of fatigue are likely complex and multifactorial. Future research should conduct large-sample prospective longitudinal studies controlling for confounders to explore contradictory factors and clarify causal relationships. Fatigue is an important symptom in COPD patients that deserves more attention from nursing staff in both research and clinical practice, and should be included in routine nursing assessments. Developing personalized interventions to effectively improve fatigue symptoms remains a challenging task that requires collaboration between clinicians and researchers.

Author Contributions

Wang Tong was responsible for conceptualization, design, and manuscript writing and revision. Quan Haishan oversaw study implementation, feasibility analysis, quality control, and final approval, taking overall responsibility and supervision. Tian Bowen and Cui Qianqian conducted literature screening and organization. Li Ying, Liu Yao, and Zhu Huahua performed data extraction and organization. All authors approved the final manuscript.

Conflict of Interest

The authors declare no conflict of interest.

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Note: Figure translations are in progress. See original paper for figures.