Applied Nursing Research 45 (2019) 23–29

Contents lists available at ScienceDirect

Applied Nursing Research

journal homepage: www.elsevier.com/locate/apnr

Original article

Symptom clusters in chronic obstructive pulmonary disease: A systematic review☆

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ARTICLE INFO

Keywords:
Symptom cluster
COPD
Respiratory-distress
Physiological-distress

ABSTRACT

Aim: To conduct a comprehensive literature review to identify symptom clusters commonly present in Chronic obstructive pulmonary disease (COPD) patients.
Background: COPD is the fourth leading cause of death worldwide. Substantial research has been studied regarding single symptoms that burden patients with this disease and the profound impacts that these symptoms can have on physical and psychological health. However, these symptoms rarely occur in isolation and limited research has been conducted identifying clinically significant relationships or clusters of symptoms associated with COPD afflicted patients.
Methods: PubMed, Web of Science, and Embase databases were used to identify potential articles limited to records published between 2005 and 2018 with human-conducted trials on adults with COPD, examining symptom clusters in this population. Only 5 studies met inclusion criteria.
Results: Across the five studies, 596 participants were included with a mean age of 70.49. Two themes emerged including psychological symptom clusters and respiratory-related symptom clusters. Anxiety-related symptoms appeared to be a common theme among psychological symptom clusters and varied greatly based on instrument selection. Inconsistent results were found in respiratory-related symptom clusters, but included difficulty breathing as a common symptom component. Only one study examined for stability of symptoms over time.
Conclusion: There were inconsistent results across all studies which may be contributed to the heterogeneity amongst patients, instruments administered, and statistical approach. Future research should be conducted to further elucidate COPD related symptom clusters, their effects on somatic and cognitive health, and the stability of these symptom clusters over time.

1. Introduction

Chronic obstructive pulmonary disease (COPD) is currently the fourth leading cause of death worldwide and is projected to be the third by the year 2020 (Global Initiative for Chronic Obstructive Lung Disease [GOLD], 2018). COPD is characterized by persistent airflow limitation associated with a chronic inflammatory response that ultimately leads to the development of respiratory symptoms and decline in lung function (GOLD, 2018). Although a respiratory disease in nature, COPD will cause patients to experience an array of unpleasant symptoms - both physical and psychological. As the disease progresses, patients will begin to experience changes in both functional and cognitive performance. Substantial research has been conducted on single symptoms, including dyspnea (Mularski and Rocker, 2015), cough (Lindberg et al., 2015), and fatigue (Kentson et al., 2016). However, there has been limited research in identifying clusters and/or relationships between multiple symptoms. Symptoms rarely occur in isolation within this population. For example, a cross-sectional study identified the symptom burden experience in COPD patients with moderate to severe airflow limitations and found a mean of 7.9 (± 4.3) associated symptoms (Eckerblad et al., 2014). The most consistently documented symptoms include dyspnea, fatigue, anxiety, and depression (Lee et al., 2018); however, identification of relationships between these symptoms is limited.

Clinically important, symptoms often have bidirectional consequences between physical and psychological stress, complicating

☆ This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors
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https://doi.org/10.1016/j.apnr.2018.11.003
Received 21 September 2018; Received in revised form 16 October 2018; Accepted 5 November 2018

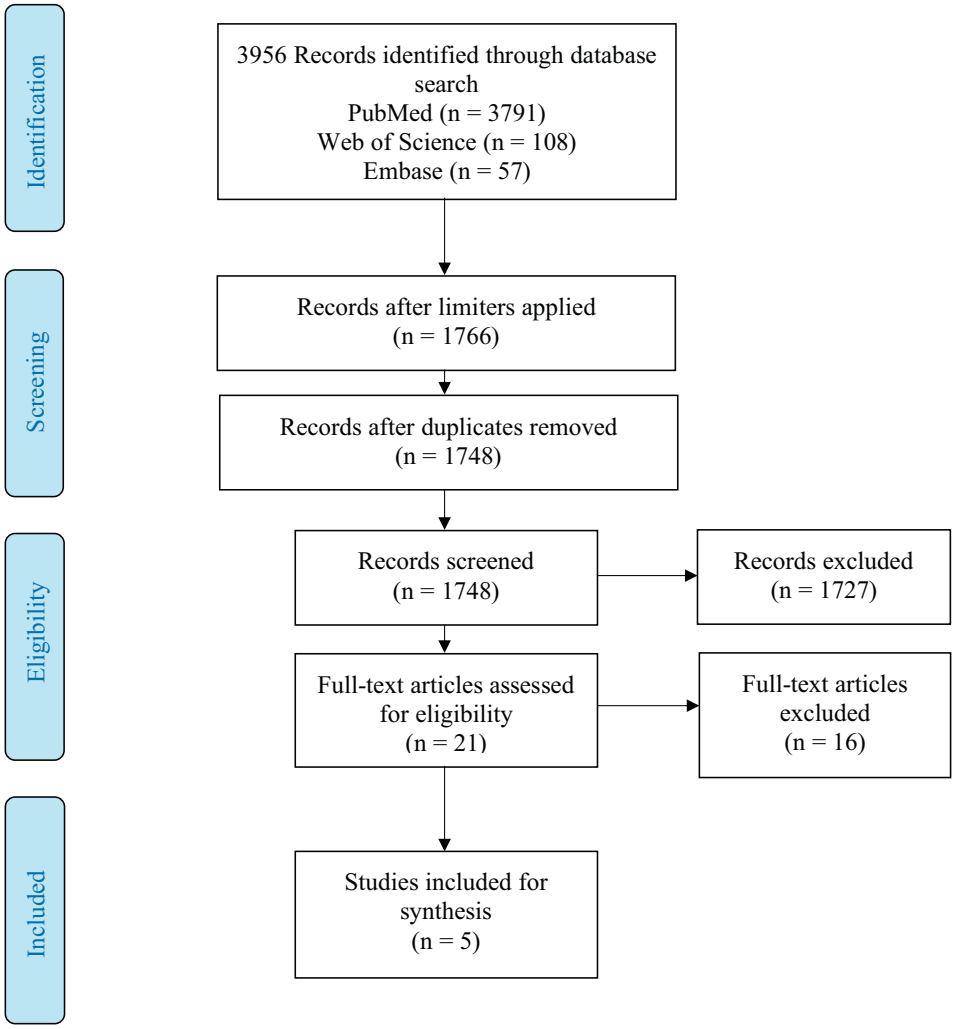

Fig. 1. PRISMA flowchart for study selection.

symptom management strategies and reducing patients' quality of life (Lee et al., 2018). For example, Bringsvor et al. (2018) found that higher symptom burdens in COPD patients strongly affected their social functioning, health-directed activities, and active engagement in life. To date, limited research has been completed on symptom clusters, especially within the COPD population (Miaskowski et al., 2017). Since COPD patients present with multiple symptoms, the clinical utility of examining for symptom clusters can provide untapped knowledge in clinically addressing multiple symptoms. In addition, symptom cluster science may be used to identify and treat distinct subgroups or phenotypes of patients with particular symptoms (Barsevick, 2016).

Several studies have attempted to identify COPD phenotypes with the aim of delivering precision medicine (Chen et al., 2014; da Silva et al., 2016; Lange et al., 2016). A literature review of COPD phenotypes by Pinto et al. (2015) identified two distinct phenotypes: one representing a younger population having lower nutritional health status with severe respiratory limitations and the other an older population with moderate respiratory limitation and increased prevalence of metabolic syndrome. Similar findings in a cross-sectional study by Christensen et al. (2016) identified three COPD subgroups ranging from low, intermediate, and high symptom experience. Patients within the high subgroup experienced the greatest occurrence of both respiratory and psychological symptoms, were found to be younger, and had a higher annual rate of acute exacerbations than those in the low and intermediate groups (Christensen et al., 2016). Nevertheless, identifying clusters of symptoms may aid in early treatment of disease. For example, Sanchez-Morillo et al. (2015) administered daily symptom questionnaires via a mobile health system in an effort to reduce the economic burden associated with hospital readmission rates from acute exacerbation of respiratory symptoms in COPD sufferers. By integrating pattern recognition software, the authors identified 31 out of 33 exacerbations 4.5 days early on average, thus reducing readmission rates by detecting unique symptom clusters (Sanchez-Morillo et al., 2015). Furthermore, the science can aid in identifying underlying etiologies and interrelationships between symptoms (Barsevick, 2016). With this knowledge, it could allow for new, innovative interventions to be developed to target multiple symptoms.

There is a robust amount of literature on identifying symptom clusters in other diseases, including prostate cancer (Lemanska et al., 2018), breast cancer (Sullivan et al., 2018), lung cancer (Wong et al., 2017), and heart failure (Yu et al., 2017). However, there is a significant gap in identifying symptom clusters in the COPD population. A review of current literature is needed to support the development of future biobehavioral targeted interventions. To the author's current knowledge, there is a lack of evidence for an integrative literature review on symptom clusters within the COPD population. Therefore, a literature review was conducted using a systematic approach to evaluate current evidence on symptom clusters in the COPD population. The findings of this review will be reported and synthesized to help healthcare providers identify symptom clusters to improve symptom management strategies.

2. Methods

The combination of PubMed, Web of Science, and Embase databases were scanned in this literature review. Search terms included symptom, symptom cluster, symptom combination, chronic obstructive pulmonary disease, and chronic obstructive lung disease. Boolean operators "OR" and "AND" were used to produce a sufficient but accurate search strategy. Truncation was applied to certain search terms to collect a variety of tense and spelling preferences. Manuscripts that examined for symptom clusters in the COPD population were reviewed. Using a systematic approach, 3956 potential articles were retrieved from the three databases listed previously. Results were then limited to records published between 2005 and 2018 that were written in English and featured human-conducted trials on adults (age > 19), leaving 1766 articles. After careful examination of potential articles, 18 duplicates were removed, leaving 1748. Those records were then screened for further eligibility. Eligible studies included those that analyzed for either primary or secondary aims of symptom clusters in COPD subjects, which left 21 full-text articles. Sixteen additional articles were then excluded based on abstracts, dissertations, general commentary articles, and COPD phenotypes. After an extensive review process of each article, 5 studies met inclusion criteria (Fig. 1).

3. Results

3.1. Overview of studies

In general, the five studies included in this review varied in design and methodology with four cross-sectional descriptive studies (Breland et al., 2015; Lim et al., 2017; Park et al., 2012; Srirat et al., 2014) and one prospective descriptive design (Srirat et al., 2015). All studies included examined symptom clusters within the COPD population with specific aims varying across studies (Table 1). Instruments used for cluster analysis were inconsistent across studies (Table 1). Instruments included the Beck Anxiety Inventory (BAI) (Breland et al., 2015), Memorial Symptom Assessment Scale (MSAS) (Park et al., 2012), and the Bronchitis Emphysema Symptom Checklist (BESC) scale (Srirat et al., 2014, 2015). Only one study included more than one instrument in cluster analysis, as seen in Table 1 (Lim et al., 2017).

3.2. Sample demographics

Across all five studies, a total sample size of 596 participants ranged from 54 to 250 per individual study. Overall, the mean age was 70.49 comprised of 481 (80.7%) males and 115 (19.3%) females. None of the studies reported baseline pulmonary function tests to confirm diagnosis or identify COPD severity. Alternatively, two studies confirmed COPD with International Classification of Disease codes (Breland et al., 2015; Lim et al., 2017). In addition to Lim et al. (2017), two other studies collaborated with physicians who confirmed COPD diagnosis and provided COPD staging (Srirat et al., 2014, 2015). One study did not report how a diagnosis of COPD was confirmed, with no data on medical coding or spirometry readings (Park et al., 2012). Due to missing data, it is difficult to determine the overall severity of the population. However, both Lim et al. (2017) and Srirat et al. (2014) reported COPD severity, based on spirometry results, as moderate ($50\% \leq FEV_1 < 80\%$ predicted) to severe airflow limitation ($30\% \leq FEV_1 < 50\%$ predicted) (GOLD, 2018).

3.3. Sample selection and study design

Recruitment strategies for the five included studies varied considerably and primarily consisted of convenience and purposive sampling through university and Veteran Affairs hospitals and pulmonary clinics. Locations of recruitments were predominately from the eastern hemisphere, including northern Thailand (Srirat et al., 2014, 2015) and South Korea (Lim et al., 2017), and two within the United States (U.S.) of America (Breland et al., 2015; Park et al., 2012). Eligibility across studies also varied based on age, diagnosis, symptom severity, and ethnicity. Of the five studies, only two included age requirements of ≥20 (Park et al., 2012) and ≥35 (Srirat et al., 2014, 2015). Breland and colleagues (2015) inclusion criteria required participants to have some form of COPD-related functional impairment and positive BAI anxiety scores. Breland et al. (2015) also was the only study to include asthma patients, compared to the other studies who excluded any other form of respiratory disorders. Lastly, Park et al. (2012) only included adult Korean immigrants to the U.S. and Srirat et al. (2014) only included participants' from Thailand.

3.4. Symptom cluster analyses

3.4.1. Psychological symptom clusters

Several symptom clusters evolved throughout these studies based on the type of instrument used for analysis and statistical methodology. Focusing on anxiety-related symptoms, Breland et al. (2015) discovered four anxiety symptom clusters. Those anxiety symptom clusters included general somatic distress, fear, nervousness, and respiration-related distress (Breland et al., 2015). Items most reflective of anxiety that factor loaded to fear from the BAI were feeling scared, fear of dying, terrified, fear of worst happening, and fear of losing control (Breland et al., 2015). Along the same spectrum of anxiety, Srirat et al. (2014) examined symptom clusters of distress using the BESC. Seven clusters emerged which the authors labeled emotional problems, memory function decline, respiratory difficulty, fatigue-related disease, sleep alteration, pain and unpleasant sensation, and respiratory muscle weakness (Srirat et al., 2014). Later, Srirat et al. (2015) reanalyzed symptom clusters over time and identified seven similar clusters; see Table 1 for symptom composition of each cluster. Similar to Breland and colleagues' results, symptoms that clustered with emotional problems were feelings of panic, anxiousness, feeling helpless and hopeless, frightened, and scared (Srirat et al., 2015). Park et al. (2012) also found similar results in their cluster analysis which included worrying, feeling nervous, feeling sad, difficulty sleeping, numbness and tingling in the hands and feet, and shortness of breath. Utilizing more than one instrument in analysis, Lim et al. (2017) identified three symptom clusters, including respiratory function, mood, and fatigue-sleep which accounted for a total variance of 71.3%. Interestingly, only anxiety and depression factor loaded to mood cluster and accounted for 17.3% total variance.

3.4.2. Respiratory-related symptom clusters

In Breland et al. (2015) cluster analysis, respiratory-related distress included feelings of choking, indigestion or discomfort in the abdomen, face flushed, and difficulty breathing. In comparison, Srirat et al. (2014) respiratory difficulty cluster included shortness of breath, shallow breathing, hard to breathe, gasping for breath, numbness, and mucus congestion which is consistent with current literature on respiratory-related symptomology in COPD population. Srirat et al. (2015) also identified respiratory difficulty as the most distressing symptom, which was likely to contribute to higher levels of emotional problems, including anxiousness, in their analysis. Lim et al. (2017) also found similar results with Srirat and colleagues' respiratory symptom cluster. Three symptoms, including dyspnea, physical functional status, and dry mouth factor loaded onto a respiratory function cluster and accounted for 39.7% of total variance.

3.4.3. Symptom cluster stability

An important concept in identifying symptom clusters is examining the stability over time. Only one study examined for similarity and stability of symptom clusters with focus on distress and severity as the two dimensions of symptom experience (Srirat et al., 2015). Evaluated over two 4-week intervals, Time 1 produced six clusters that had similar

Table 1
Symptom clusters analyses.

Study (year), study aim and design	Analytical method	Assessment tools	Patients (N) and sample characteristics	Symptom cluster(s)	Composition of symptom cluster(s)	Additional findings
Park et al. (2012) Evaluate symptom burden, symptom clusters, relationship between those symptoms and functional performance.	EFA – oblique rotation HCA MLA	Cluster analysis MSAS Predictors of relationships between symptoms and functional performance VAS, MMRC, POMS-SF, mMOS-SS, SL-ASIA, and FPI-SF	N = 54 Mean age = 75 ± 7.1 Male = 90.7%	Cluster 1 Cluster 2 Cluster 3	Cluster 1 Worrying, feeling nervous, feeling sad, difficulty sleeping, numbness/tingling in hands/feet, shortness of breath Cluster 2 Feeling bloated, dizziness, feeling drowsy, lack of energy, cough, dry mouth, sweats, pain Cluster 3 Problems with urination, constipation	Functional performance was most related with dyspnea alone in the MSAS total score, symptoms of MSAS, MMRC, and VAS, $r = -0.29$, $r = -0.27$, $r = -0.43$, $r = -0.27$, respectively.
Srirat et al. (2014) Identify symptom clusters, symptom distress, and best management practices to treat clusters.	PCA - orthogonal rotation Descriptive statistics	Cluster analysis PIQ and BESC** Identify effective management practices SMSQ	N = 250 Thais Mean age = 71.03 ± 7.16 Male = 67.2%	Cluster 1: Emotional problems Cluster 2: Memory function Cluster 3: Respiratory difficulty Cluster 4: Fatigue-related distress Cluster 5: Sleep alteration Cluster 6: Pain and unpleasant sensation Cluster 7: Respiratory muscle weakness	Mean distress levels ranked highest to lowest within the following five symptom clusters Cluster 3: Respiratory difficulty Hard to breath, short of breath, shallow breathing, mucus congestion, gasping for breath Cluster 4: Fatigue-related distress Fatigue, exhaustion, no energy Cluster 5: Sleep alteration Poor sleep, trouble falling asleep, disturbed sleep Cluster 6: Pain and unpleasant sensation Leg aches, cramps, pins and needles feelings, pain in other region Cluster 1: Emotional problems Feel like I need air, worried about getting air, edgy, upset, lonely, feel hopeless, feel helpless	Hard to breath showed the highest level of mean distress. Eight out of 30 symptoms were prevalent in 100%. The eight symptoms are as follows and represent the mean distress level from highest to lowest: fatigue, short of breath, shallow breathing, exhaustion, feel like I need air, mucous congestion, coughing, and worried about getting air. Clusters and best treatments Cluster 1 - Bronchodilator and pursed lip breathing Cluster 2 - Bronchodilator and reduced activities Cluster 3 – Alprazolam and listening to music Cluster 4 – Nonsteroidal anti-inflammatory drug and paracetamol Cluster 5 – Amitriptyline and fate acceptance and getting used to symptoms
Breland et al. (2015) Identify factor structure of BAI, symptom clusters, and quality of life in COPD population.	PCA – oblique rotation MLA	Cluster analysis BAI Model prediction for quality of life domains CRQ, MRC, and PHQ-9	N = 162 Veterans Mean age = 66.46 ± 8.94 Caucasian = 68% Male = 94%	Cluster 1 General somatic distress Cluster 2 Fear Cluster 3	Cluster 1 Dizziness or lightheaded, faint, unsteady, wobbliness in legs, heart pounding or racing Cluster 2 Scared, fear of dying, terrified, fear of worst happening, fear of losing control Cluster 3 Shaky, hand trembling, nervous, unable to relax Cluster 4	Three regression models predicted quality of life domains. Model 1: Predicting mastery over COPD Fear cluster, depression symptoms, and COPD functional impairment revealed a negative association with mastery over COPD Model 2: Predicting dyspnea-related quality of life Severity of functional impairment predicted worse dyspnea-related quality of life

(*continued on next page*)

Table 1 (*continued*)

Study (year), study aim and design	Analytical method	Assessment tools	Patients (N) and sample characteristics	Symptom cluster(s)	Composition of symptom cluster(s)	Additional findings
				Nervousness Cluster 4 Respiratory-related distress	Feeling of chocking, indigestion or discomfort in the abdomen, face flushed, difficulty breathing, numbness or tingling, feeling hot, sweating (not due to heat)	Model 3: Predicting fatigue-related quality of life Higher depression symptoms predicted worse fatigue-related quality of life
Srirat et al. (2015) Analyze stability and similarity (severity and distress) of clusters over time	PCA - orthogonal rotation Descriptive statistics Secondary data*	Cluster analysis PIQ and BESC** Symptom similarity and stability over time Numerical rating system	N = 250 Thais Mean age = 71.03 ± 7.16 Male = 67.2%	Clusters at Time 1 Cluster 1: Emotional problems Cluster 2: Memory function Cluster 3: Disease-related fatigue Cluster 4: Respiratory difficulty Cluster 5: Sleep alteration Cluster 4: Fatigue-related distress Cluster 6: Pain and unpleasant sensation Cluster 7: Chest discomfort	Clusters at Time 2 Cluster 1: Feel like a cripple, panicky, anxious, …20 more symptoms Cluster 2: Forget recent things, forgetful, poor memory, difficulty remembering Cluster 3: Exhaustion, fatigue, no energy, upset Cluster 4: Short of breath, shallow breathing, hard to breath, numbness Cluster 5: Poor sleep, trouble falling asleep Cluster 6: Pins and needles feeling, cramps, leg aches, pain at other regions, tingling in arms and legs Cluster 7: Chest tightness, chest filled up, mucous congestion	The similarity rate of severity and distress in each cluster ranges from 75% to 100% at Time 1. Conversely, the similarity rate of both dimensions increased replication from 95.4% to 100% at Time 2. Lastly, replication rate for distress clusters ranged from 66.7% to 100%. Replication rate of respiratory difficulty cluster was 50%. Back-and-forth transitions between psychological and physical symptoms within clusters over time were observed.
Lim et al. (2017) Identify symptom clusters, explore relationships between symptoms clusters and clinical traits, and explore the their effects on quality of life	PCA – varimax rotation K-means cluster analysis	Cluster analysis FACIT, BDI, STAI, Korean Sleep Scale A, visual analog scale for dry mouth; KPS, patient demographics, clinical traits, Borg scale, and visual analog scale for dry mouth Quality of life analysis CCQ	N = 130 patients located in South Korea Mean age = 69.5 ± 8.7 Male = 86.2%	Cluster 1: Respiratory-functional cluster Cluster 2: Mood cluster Cluster 3: Fatigue-sleep cluster	Cluster 1: Respiratory-functional cluster Dyspnea, physical functional status, and dry mouth Cluster 2: Mood cluster Anxiety and depression Cluster 3: Fatigue-sleep cluster Sleep disorder and fatigue	Taking into account the patients symptom clusters, clinical traits, and quality of life, two distinct subgroups emerged; identified as Low-symptom subgroup and High-symptom subgroup. Patients in the High-symptom subgroup within all three clusters had significantly poor quality of life. High-symptom subgroup was older, experienced high levels of symptoms, had lower educational level and monthly income.

Note. BAI, Beck Anxiety Inventory; BDI, Beck Depression Inventory; BESC, Bronchitis Emphysema Checklist; CCQ, Clinical COPD Questionnaire; CRQ, Chronic Respiratory Disease Questionnaire; EFA, Exploratory factor analysis; FACIT, Functional Assessment of Chronic Illness Therapy-Fatigue; FPI-SF, Functional Performance Inventory-Short Form; HCA, Hierarchical cluster analysis; KPS, Karnofsky Performance Scale; MLA, Multiple linear regression; mMOS-SS, modified Medical Outcomes Study Social Support Survey; MMRC, Modified Medical Research Council Dyspnea Scale; MRC, Medical Research Council Dyspnea Scale; MSAS, Memorial Symptom Assessment Scale; PCA, Principle Component Analysis; PHQ-9, Patient Health Questionnaire-9; PIQ, Personal Information Questionnaire; POMS-SF, Profile of Mood States-Short Form; SL-ASIA, Suinn-Lew Asian Self-Identity Acculturation Scale; SMSQ, Symptom Management Strategies Questionnaire; STAI, State-trait Anxiety Inventory; VAS, dyspnea Visual Analogue Scale *Secondary data **Modified scale.

results on both dimensions, ranging from 75% to 100%. For example, in cluster 1 (titled emotional problems), symptoms of 'feel like a cripple,' panicky, and anxious showed similar results in terms of symptom severity and distress. Time 2 revealed five clusters with a similarity rate ranging from 95.4% to 100%. Important with respect to identifying a symptom cluster, stability over time points showed six clusters with five of them meeting the acceptable replication rate of 75%. Clusters of stability included emotional problems (79.1%), memory function decline (100%), chest discomfort (100%), pain and unpleasant sensation (80%), and sleep alteration (100%). To note, respiratory difficulty cluster had a replication rate of 50%. Most notably, there were back-and-forth transitions between psychological and physical symptoms within clusters. For example, the authors highlighted that at Time 1, symptoms of 'feel like I need air' and 'worried about getting air' factored into emotional problems, but at Time 2, symptoms loaded on respiratory difficulty cluster.

4. Discussion

The aim of this literature review was to evaluate the current evidence of symptom clusters in COPD population. In this review, several symptom clusters emerged that included both physical and psychological symptoms. As highlighted, there was considerable overlap of somatic and cognitive symptoms across studies, especially regarding anxiety. Interestingly, Breland et al. (2015) found that fear-related items on the BAI showed significant correlation with regards to COPD mastery. This indicates that the greater the fear, the lower perceived COPD mastery. Furthermore, multiple regression models revealed fear symptom cluster, depression symptoms, and COPD-related functional impairment to be negatively associated with COPD mastery. The significance of these results highlight that these cognitive symptoms may be a mediator in hindering self-care management. Interestingly, only one study identified depression in a symptom cluster. Well recognized in the literature, both anxiety and depression are common comorbidities in this population (Yohannes and Alexopoulos, 2014). A recent study by Xu and Li (2018) analyzed for risk factors of depression and found that high-serum CRP and lower FEV1 were significant risk factors for onset of depression in COPD patients. Tetikkurt et al. (2011) evaluated bronchoalveolar lavage (BAL) cytology with anxiety and depressive symptoms and found an association between the severity of anxiety and depressive scores with changes in abnormal BAL cytology reports, highlighting that the extent of lung parenchyma damage may be a mediator in developing somatic symptoms.

There was considerable heterogeneity across studies, including sex, ethnicity, geographical location, and culture. As highlighted, nearly 19% of the total sample population consisted of females which included higher levels of somatic and cognitive symptoms compared to men across all studies. To note, it has reported that women are vulnerable to disease-specific changes that may exacerbate both anxiety and depressive symptoms (Hardin et al., 2016), which may contribute to different symptom clusters between sexes. In regards to location, Srirat et al. (2014) study only included participants from northern Thailand as compared to Park et al. (2012), who only included Korean immigrants, and Breland et al. (2015), who only included U.S. veterans, which may limit generalizability. Associated with geographical locations, cultural practices can often affect one's self-reported data. Park et al. (2012) reported that the frequency, severity, and distress among their sample was lower comparatively to other studies, which may be attributed to stoicism.

A major challenge in symptom cluster research is identifying empirical instruments with excellent psychometric properties and good item validity and reliability. Two studies altered question formats and also designed their own instrument, which can contribute to lower validity and reliability (Srirat et al., 2014, 2015). These modifications and inconsistencies contribute to the inability to compare and contrast outcomes of each study. Furthermore, since each study's aim guided their instrument selection, the number of symptoms analyzed varied greatly, which yields different clusters. Therefore, it is important to utilize multiple instruments that capture a variety of COPD-related symptoms to gain a true picture of symptom clusters. Furthermore, there is no "gold standard" for which statistical method should be used to analyze symptom clusters. From the five studies included in this review, a variety of analytical approaches were implemented, including principle component analysis, hierarchical cluster analysis, factor analysis, and *k* means clusters (Table 1). Due to these variations, it is difficult to provide a comprehensive analysis. Lastly, only one study completed a prospective study with two repeated measures (Srirat et al., 2015). Further longitudinal studies are warranted to establish the trajectory of disease to determine a significant result and design targeted interventions (Barsevick, 2016). Although there is inconclusive evidence to establish prevalent symptom clusters, these studies substantiate the need to anticipate, assess for, and address prevalent symptoms. To briefly mention, significant efforts were undertaken to identify related articles; there is the possibility that other pertinent studies may be absent. However, to the author's current knowledge, this literature review reflects the most recent work on symptom clusters within the COPD population.

5. Future recommendations

Recently, a workshop sponsored by the National Institute of Nursing Research titled "Advancing Symptom Science through Symptom Cluster Research" synthesized the current body of evidence on the science of symptom clusters (Miaskowski et al., 2017). Ultimately, the expert panel concluded that an operational definition of symptom cluster remains undefined (Miaskowski et al., 2017). Therefore, it is greatly recommended to continue to work collaboratively with symptom science researchers and clinicians to conceptually define a symptom cluster. Furthermore, it is imperative to validate and standardize symptom cluster instruments and methodologies to appropriately appraise and compare study findings.

Additionally, longitudinal research symptom cluster research is warranted to investigate the stability over time to develop interventions that target multiple interrelated symptoms (Dunn et al., 2017). Lastly, it is important to use multiple well-validated psychometric instruments that analyze for a variety of COPD-related symptoms, including both physical and psychological.

6. Conclusion

This literature review identified five studies that examined for symptom clusters. There was considerable overlap with both somatic and cognitive symptoms. Respiratory-related symptoms were the most distressful of all symptoms. Since COPD symptoms rarely occur in isolation, it is critical to continue to explore and identify symptom clusters to lower the symptom burden and delay disease progression.

Declarations of interest

None.

Competing interests

None.

Acknowledgements

We would like to thank Stephen Carpenter for editing and proofreading assistance.

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