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Prevalence and clinical characteristics of sleep disorders in chronic obstructive pulmonary disease: A systematic review and meta-analysis

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ABSTRACT

Background: Sleep disorders, including obstructive sleep apnea (OSA), restless leg syndrome (RLS) and insomnia, are present in chronic obstructive pulmonary disease (COPD) with varied prevalence. The aim of this systematic review and meta-analysis was to investigate prevalence of OSA, RLS and insomnia in patients with COPD and summarize their clinical characteristics.

Methods: We searched PubMed, Web of Science and Scopus for eligible articles reporting the prevalence of OSA, RLS, and insomnia in COPD patients. The Newcastle–Ottawa scale was applied for quality assessment. Odds ratios or mean differences with 95 % confidence intervals (CIs) were applied for the overall prevalence calculation and clinical characteristics assessment. Sensitivity analysis, subgroup analysis and meta-regression were conducted to evaluate the heterogeneity of the results.

Results: Sixty articles reporting the prevalence of sleep disorders in patients with COPD were included, and the prevalence of OSA, RLS, and insomnia reached 29.1 %(95%CI 27.2%–30.9 %), 21.6 %(95%CI 11.8%–33.3 %) and 29.5 %(95%CI 16.9%–44.0 %), respectively. COPD patients with OSA were characterized by male sex (OR 1.631 95 % CI: 1.231–2.161), obesity(kg/m^2) (MD 4.435, 95 % CI 3.218–5.652), higher Epworth Sleepiness Scale (MD: 3.741, 95 % CI: 0.655–6.828, $p = 0.018$), better pulmonary function (MD 5.66, 95 % CI 3.546–7.774) and higher risks of hypertension (OR 1.933 95 % CI 1.382–2.70) and diabetes (OR 1.898 95 % CI 1.264–2.849). COPD patients with RLS were associated with a higher Epworth sleepiness scale (ESS) score (MD 3.444, 95 % CI 1.880–5.008) and a longer COPD duration(year) (MD: 3.656, 95 % CI: 2.209–5.103). COPD patients with insomnia were characterized by female sex(OR 0.556, 95%CI 0.545,0.567, $p < 0.001$).

Conclusion: Our study suggests that OSA, RLS and insomnia are common in COPD patients with specific clinical characteristics. Further studies are needed to explore the interactions between COPD and sleep disorders.

1. Introduction

Chronic obstructive pulmonary disease (COPD), characterized as persistent airflow obstruction due to structural changes in airways or alveoli, is considered a heavy burden of respiratory disease worldwide [1]. It has been reported that COPD prevalence has reached 10.3 % (95 % confidence interval (CI) 8.2–12.8) worldwide and 8.6 % (95 % CI 7.5–9.9) in China [2,3]. COPD is also regarded as the fourth leading cause of years of life lost (YLLs) globally with a series of comorbidities, including cardiovascular diseases, osteoporosis, and pulmonary hypertension [4,5]. The huge burden and comorbidities pose a great challenge for effective intervention in COPD patients.

Accounting for one-third of human life, sleep plays an important role in the maintenance of multisystem homeostasis [6]. Sleep disorders, including obstructive sleep apnea (OSA), insomnia and restless leg syndrome (RLS), are considered essential comorbidities of COPD [7]. Previous studies have shown that sleep disorders exert a negative impact on the prognosis of COPD patients. Shi et al. pointed out that both OSA

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and insomnia are associated with increased susceptibility to acute exacerbation of COPD (AECOPD) [8]. Shah et al. suggested that COPD-OSA overlap is associated with a higher risk of hypertension (OR 1.68, 95 % CI 1.21–2.35) than COPD alone [9]. However, the prevalence of different sleep disorders in patients with COPD varies widely in different studies, and the clinical characteristics of COPD patients with sleep disorders remain largely unknown.

Therefore, this meta-analysis aims to provide a pooled prevalence of OSA, insomnia, and RLS in COPD patients and then summarize their clinical characteristics.

2. Methods

This meta-analysis was registered on the INPLASY website (INPLASY202330057) and performed according to the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) [10] and the Meta-analysis of Observational Studies in Epidemiology (MOOSE) [11] guidelines.

2.1. Literature search

Two investigators (DRD and GYZ) independently searched PubMed, Web of Science and Scopus for eligible studies from the inception of the databases to March 2023. The main search strategy is provided in Table S1. References of related reviews and meta-analyses were also manually screened to prevent omissions.

2.2. Study selection

The inclusion criteria were as follows: (1) Studies reporting both COPD patients with OSA, insomnia and RLS and patients suffered from COPD alone. (2) A sample size of over 50 was used to avoid potential bias. (3) Observational studies, such as cross-sectional, cohort and case–control studies. (4) Reporting appropriate criteria to diagnose COPD and sleep disorders, including objective tests(such as spirometry examination for COPD and polysomnography(PSG) for OSA), International Classification of Diseases (ICD) codes and medical records. The exclusion criteria were as follows: (1) Duplicated data published by the same institution or from the same database. In this case, only the study with the largest population was enrolled for analysis. (2) Studies not published in English. (3) Studies with obvious selection bias of COPD patients (like only include COPD patients in acute exacerbation period). Two authors (DRD and GYZ) independently screened the retrieved articles, and any disagreements were resolved by a third author (YCS).

2.3. Data extraction and quality assessment

The following characteristics were extracted for further analysis: author, publication year, country, study type, study location (hospital or community), diagnostic criteria of COPD and sleep disorders, number and baseline data of COPD patients with and without sleep disorders. The quality of eligible studies will be evaluated independently by two authors (DRD and GYZ) independently using the Newcastle–Ottawa Scale (NOS), which is composed of “selection”, “comparability” and “exposure”. The total scores are divided into “high quality (7–9)”, “moderate quality (4–6)” and “low quality (0–3)”.

2.4. Statistical analysis

The pooled prevalence with 95 % confidence intervals (CIs) to assess the proportion of OSA, insomnia, and RLS in COPD patients was calculated. The results were reported as pooled prevalence with 95 % CIs. For clinical characteristics, those that were reported in more than three articles were calculated. The dichotomous variables are presented as odds ratios (ORs) with 95 % CIs, while the continuous variables are presented as the mean difference (MD) with 95 % CIs. Heterogeneity was measured using the Q test and I square (I^2) statistic. If significant heterogeneity ($p < 0.05$ of Q test or $I^2 > 50$ %) was obtained, we applied a random effects model; otherwise, a fixed effects model was used instead. Sensitivity analysis, subgroup analysis and meta-regression were conducted to investigate the source of heterogeneity. All analyses were performed using Stata (version 16.0), and a p value < 0.05 was considered statistically significant.

3. Results

3.1. Study screening and characteristics

As shown in Fig. 1, a total of 14,000 records were identified after screening, with 9132 records left after removing duplicates. After primary screening and full-text assessment, 60 eligible articles were enrolled for further analysis. Baseline characteristics of the eligible articles are presented in Table S2.

3.2. Quality assessment

The results of the quality assessment among 60 eligible studies are presented in Table S2, ranging from 6 to 7. All studies enrolled in our meta-analysis were of moderate to high quality.

3.3. Pooled prevalence of sleep disorders in COPD patients

In total, 42 articles reported OSA prevalence (2.7%–73.9 %) [12–53], 12 articles reported RLS prevalence (3.0%–36.8 %) [53–64], and 12 articles reported insomnia prevalence (2.1%–69.9 %) [19,33,34,53,61,65–71]. The pooled prevalence of OSA, RLS and insomnia were 29.1 % (95%CI 27.2%–30.9 %), 21.6 %(95%CI 11.8%–33.3 %) and 29.5 %(95%CI 16.9%–44.0 %) respectively(Fig. 2). Significant heterogeneity was observed among the pooled prevalence of OSA(99.88 %), RLS (98.57 %) and insomnia(99.80 %).

3.4. Clinical characteristics and heterogeneity assessment of OSA

COPD patients with OSA were characterized as male sex (OR: 1.631, 95 % CI: 1.231–2.161, $p = 0.001$), body mass index (BMI)(kg/m^2) (MD: 4.435, 95 % CI: 3.218–5.652, $p < 0.001$), percentage of forced expiratory volume in 1 s (FEV_1%) (MD 5.56, 95 % CI:1.279–9.842 $p = 0.011$), higher Epworth sleepiness score (ESS) (MD: 3.741, 95 % CI: 0.655–6.828, $p = 0.018$), risk of hypertension (OR 1.933, 95 % CI: 1.382–2.703 $p < 0.001$) and diabetes mellitus (OR 1.898 95 % CI: 1.264–2.849 $p = 0.002$) compared to those without OSA(Table 1). No significant difference was observed in age, number of centers, PaO2, PaCO2, smoking (ever), smoking (current) or risk of coronary disease. Sensitivity analysis showed that studies authored by Javier et al. [46], Jessica et al. [44] and Luyster et al. [53] may become a source of heterogeneity (Fig. S1). In the subgroup analysis, we found that the OSA prevalence in cross-sectional studies (35.3 %, 95 % CI: 27.3%–43.7 %) was higher than that in cohort(23.4 %,95%CI 20.3%–26.7 %) and case–control studies(13.0 %, 95%CI 7.1%–21.2 %). Moreover, subgroup differences were observed among different diagnostic criteria ofOSA (Table 2). The results of the meta-regression showed that age, male proportion, smoking status, PaO2, PaCO2, pulmonary function, ESS score, risk of hypertension, diabetes mellitus, coronary disease and pulmonary hypertension were not sources of heterogeneity, while the risk of depression showed a significant result($p = 0.008$) (Table 3).

3.5. Clinical characteristics and heterogeneity assessment of RLS

COPD patients with RLS were characterized as a higher Epworth sleepiness scale (ESS) score (MD: 3.444, 95 % CI: 1.880–5.008) and a longer COPD duration(year) (MD: 3.656, 95 % CI: 2.209–5.103) compared to those without RLS. No significant difference was observed

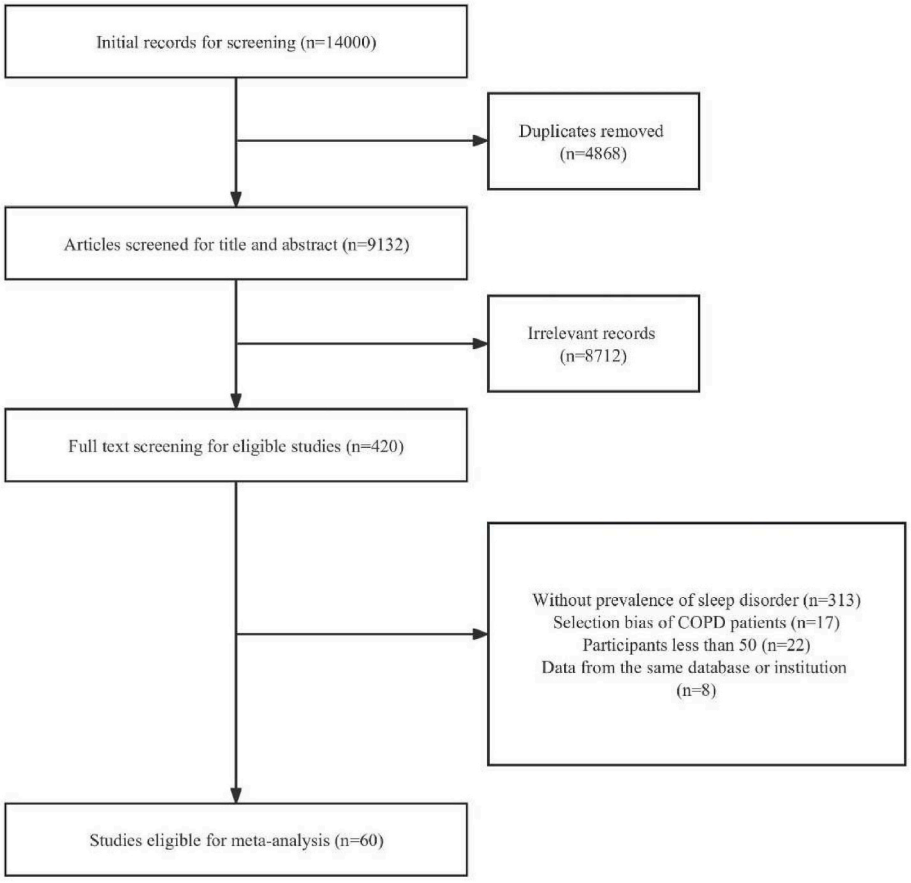

Fig. 1. Flow chart of literature search and selection.

in age, sex, FEV1%, smoking, PaO2, PaCO2, body mass index (BMI) or serum iron(Table 1). Sensitivity analyses showed that the results were stable after the leave-one-out process (Fig. S2). Subgroup analyses showed consistent results among studies with different geographic positions, different numbers of centers, and different diagnostic criteria for COPD. However,. those patients diagnosed with International RLS Study Group (IRLSSG) criteria showed a higher RLS prevalence than those diagnosed with other non-IRLSSG criteria(27.8 % vs 10.8 %) (Table 2). The results of the meta-regression showed that RLS prevalence did not vary significantly with publication year, sex, age, BMI, and smoking (packs/year) (all $p > 0.05$)(Table 3).

3.6. Clinical characteristics and heterogeneity assessment of insomnia

COPD patients with insomnia were characterized as female sex(OR 0.556, 95%CI 0.545,0.567, $p < 0.001$), while no significant difference was observed in age(Table 1). Sensitivity analysis showed stable results during the leave-one-out process (Fig. S3). Subgroup analysis showed no significant difference between studies in continent, number of centers or diagnostic criteria of COPD (Table 2). Meta-regression indicated that age, proportion of males, BMI, smoking (ever) and smoking (current) were not responsible for heterogeneity (all $p > 0.05$) (Table 3).

4. Discussion

Sleep disorders, including OSA, RLS and insomnia, have become serious health problems worldwide. Adam et al. reported that approximately 14 % of the global population was affected by OSA [72]. Mauro et al. pointed out that the prevalence of RLS ranged from 1% to 3% in Asian populations and 5 % to 13 % in European and North American populations [73]. Another international multi-center study reported that 11.3 % of the participants were diagnosed with short-term sleep disorders [74]. Our results indicated that the prevalence of OSA, RLS and insomnia in COPD patients reached 29.1 %, 21.6 % and 29.5 %, respectively, respectively. Therefore, despite a lack of double-armed analysis due to insufficient data, we still assume that the prevalence of OSA, RLS and insomnia in COPD is higher than that in the overall population, which can be caused by several potential mechanisms.

The possible mutual relationships between COPD and sleep disorders are presented in Fig. 3. OSA is characterized by upper airway collapse and hypoventilation, resulting in hypoxemia, snoring and other symptoms [75]. Current evidence and our results indicate that COPD exerts a prominent promoting rather than inhibiting effect on OSA development. For OSA-promoting factors, skeletal muscle dysfunction may serve as a possible cause of OSA development, as 15.5 % of COPD patients were reported to suffer from sarcopenia [76]. Muscle dysfunction is related to pharyngeal muscle weakness, leading to gas exchange disorder in the upper airways and finally causing OSA [6]. Another possible reason for the higher OSA prevalence in COPD patients is rostral fluid shift [77], a common pathological feature in severe COPD patients who have progressed to pulmonary heart disease, which is associated with fluid accumulation in the neck region, causing airway narrowing and OSA development [77]. However, there are also COPD-related factors inhibiting OSA development. Samuel et al. observed a negative correlation between emphysema severity and OSA progression in smokers from the COPDGene cohort, probably caused by tracheal caudal traction and transpulmonary pressure elevation [78]. The results of this study indicated that the COPD-OSA relationship may be associated with the COPD phenotype. Sleep architecture alterations in COPD patients may also influence OSA pathogenesis, which can be attributed to the association between COPD and sleep rhythm disorders [79] leading to symptoms similar to OSA in COPD patients, thereby aggravating OSA

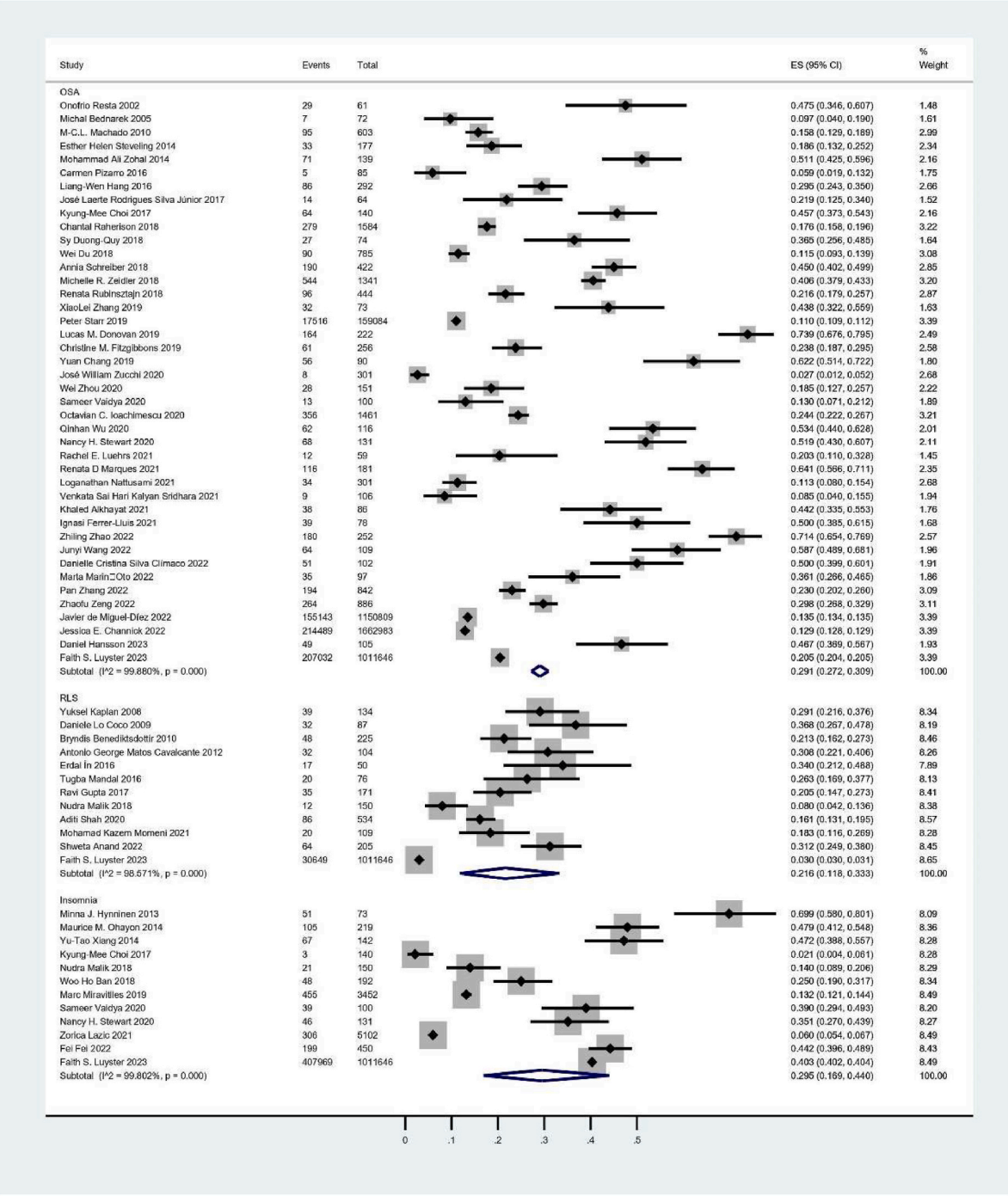

Fig. 2. Prevalence of OSA, RLS and insomnia in COPD patients.

progression. Additionally, OSA also exert a complex impact on COPD pathogenesis. OSA may induced hypoxemia and muscular weakness, which may promote COPD development [80], while severity of OSA is negatively correlated with emphysema progression [78]. RLS is a sensorimotor disorder characterized by an uncontrollable urge to move legs, which may serve as an important comorbidity in multiple diseases [73]. Growing clinical and experimental evidence suggests that iron deficiency in the central nervous system and dysfunction in the dopaminergic system are closely associated with RLS development, which may be accelerated in COPD patients [81]. It is clear that iron homeostasis is affected in COPD patients, causing iron overload in lung tissue and sputum and leading to iron deficiency due to hepcidin overexpression [82]. In addition, hypoxia induced by COPD may participate in RLS pathogenesis by activating the hypoxia inducible factor-1(HIF-1) pathway, which upregulates tyrosine hydroxylase and vascular endothelial growth factor(VEGF) expression, affecting the function of the dopaminergic system [73,83]. Hypoxia also activates iron uptake genes such as divalent metal transporter 1 and protein transferrin receptor 1 in enterocytes, which may affect iron delivery and homeostasis [84,85]. Furthermore, chronic inflammation in COPD is able to regulate iron metabolism by inhibiting iron release from the duodenum, leading to iron deficiency [84]. In addition, inflammatory cytokines may cause dopamine neuron dysfunction after crossing the blood–brain barrier, contributing to dopamine metabolism disruption [86]. In patients with COPD, irritants such as tobacco smoke activate airway epithelial cells and release proinflammatory mediators such as chemokine

Table 1
Clinical characteristics of OSA and RLS in COPD patients.

Clinical characteristics	Number of studies	Total COPD cases	Mean difference or odds ratio(95 % CI)	I^2	OR/ MD
OSA					
Sex(male vs female)	21	1827313	1.631 (1.231,2.161) p = 0.001	99.0 % p < 0.001	OR
Hypertension	13	4020	1.933 (1.382,2.703) p < 0.001	74.3 % p < 0.001	OR
Diabetes mellitus	12	4026	1.898 (1.264,2.849) p = 0.002	69.3 % p < 0.001	OR
Smoking (current)	9	1973	0.989 (0.627,1.562) p = 0.963	66.8 % p = 0.002	OR
Smoking (ever)	7	3467	1.098 (0.905,1.332) p = 0.344	0 % p = 0.789	OR
Coronary disease	4	2202	1.227 (0.723,2.083) p = 0.448	64.7 % p = 0.037	OR
Age	22	1827374	−0.679(-1.540, 0.182) p = 0.122	98.9 % p < 0.001	MD
BMI	17	4311	4.435 (3.218,5.652) p < 0.001	91.5 % p < 0.001	MD
FEV1%	12	3381	5.56 (1.279,9.842) p = 0.011	82.6 % p < 0.001	MD
FEV1/FVC	10	2949	5.66 (3.546,7.774) p < 0.001	69.0 % p = 0.001	MD
PaCO2	7	1112	1.607(-0.198, 3.412) p = 0.081	77.0 % p < 0.001	MD
PaO2	6	1026	−1.300 (-2.781,0.182) p = 0.085	34.1 % p = 0.180	MD
ESS	6	1618	3.741(0.655, 6.828) p = 0.018	96.0 % p < 0.001	MD
RLS					
Sex(male vs female)	7	765	0.716 (0.353,1.453) p = 0.355	61.4 % p = 0.016	OR
Age	6	560	1.298 (-1.452,4.049) p = 0.355	65.4 % p = 0.013	MD
FEV1%	5	544	−8.645 (-23.727,6.437) p = 0.261	97.4 % p=<0.001	MD
Smoking (packs/ year)	5	443	5.600 (-0.331,11.531) p = 0.064	19.0 % p = 0.294	MD
PaO2	4	435	−6.463 (-19.315,6.390) p = 0.324	97.4 % p < 0.001	MD
PaCO2	4	435	4.543 (-2.762,11.849) p = 0.223	95.0 % p < 0.001	MD
BMI	4	334	−1.105 (-2.792,0.583) p = 0.200	64.3 % p = 0.038	MD
ESS	4	317	3.444 (1.880,5.008) p < 0.001	65.2 % p = 0.035	MD
Serum iron	3	359	−13.195 (-28.573,2.184) p = 0.093	85.3 % p = 0.001	MD
COPD duration	3	263	3.656 (2.209,5.103) p < 0.001	13.0 % p = 0.317	MD
FEV1/FVC	3	230	−8.352 (-17.196,0.452) p = 0.063	91.4 % p < 0.001	MD
Insomnia					
Sex(male vs female)	3	1011980	0.556 (0.545,0.567) p < 0.001	0 % p = 0.686	OR
Age	3	1011980	−2.778 (-5.873,0.317) p = 0.079	89.1 % p < 0.001	MD

CXC-chemokine ligands and tumor necrosis factors, attracting neutrophils and promoting the inflammatory response [87]. Higher levels of inflammation markers, C-reactive protein (CRP) and neutrophil-to-lymphocyte ratio (NLR), were observed in RLS patients [88], which also showed great predictive value for mortality in COPD patients [89,90]. Insomnia is a common kind of sleep disorder characterized by sleep initiation or maintenance problems leading to daytime dysfunction in patients with sufficient sleep opportunities [91]. Regarding COPD's impact on insomnia, Lowie et al. determined that sympathetic activity elevation and respiratory symptoms may result in sleep disturbance [7]. In addition, inflammatory biomarkers such as tumor necrosis factor-α (TNF-α), which plays an essential role in COPD progression, were elevated in COPD patients (p = 0.001) [92,93]. Interestingly, Qiong et al. reported that TNF-α may serve as an inducer of NOD-like receptor proteins 1 and 3, which may lead to increased inflammation levels and sleep-related neuron damage [94]. Moreover, sleep disorder breathing in COPD patients can also cause sleep deficiency due to pulmonary impairments [79]. However, whether RLS and insomnia exert an effect on COPD pathogenesis remained unclear, which need future studies to investigate.

We also observed that COPD patients with OSA are associated with male (OR: 1.631, 95%CI:1.231–2.161, p = 0.001), obesity(MD: 4.435, 95 % CI: 3.218–5.652, p < 0.001), more severe daytime sleepiness(MD: 3.741, 95%CI:0.655–6.828, p = 0.018) and higher rate of hypertension (OR 1.933, 95%CI 1.382–2.703 p < 0.001) and diabetes mellitus(OR 1.898 95%CI 1.264–2.849 p = 0.002). OSA in COPD patients was also associated with better pulmonary function (MD 5.66, 95 % CI 3.546–7.774 p < 0.001), suggesting that OSA may have a protective effect on COPD progression. This can also be explained by the negative emphysema-OSA association. In the subgroup analyses, cross-sectional were associated with a higher OSA prevalence than cohort and case-control studies, which may be attributed to potential bias caused by the study design. Interestingly, our results also showed that OSA patients diagnosed with AHI>15 were higher than those diagnosed with AHI>10 (35.4 % vs 25.2 %). However, only two articles were enrolled in the AHI>10 group, which were published in 2002 [12] and 2014 [15], while OSA prevalence increased rapidly in the 21st century due to an increasing global obesity rate [95]. In addition, compared with diagnosing OSA via polysomnography (the gold standard), those diagnosed with questionnaires presented a higher OSA prevalence (49.3 %, 95 % CI 35.3%–63.3 %), while those diagnosed with ICD criteria were associated with a lower OSA prevalence(15.4 %, 95%CI 10.4%–21.1 %). This suggests that diagnostic methods other than polysomnography still lack diagnostic accuracy due to a lack of specificity or sensitivity. In our meta-regression, we found that the proportion of depression may partly explain the source of OSA heterogeneity (p = 0.031). RLS is more common in women than in men and may be associated with iron deficiency [96]. However, we observed that there was no significant difference in sex (male vs female) or serum iron between RLS-positive and RLS-negative COPD patients, which may be because the sample size was small, and brain iron deficiency may be a better indicator of RLS than serum iron deficiency. Moreover, COPD diagnosed with GOLD criteria and RLS diagnosed with IRLSSG criteria were associated with a higher

Table 2
Subgroup analysis of sleep disorders prevalence in COPD patients.

Subgroups	Number of studies	Pooled prevalence(95 % CI)	z(p)	I^2(p)
OSA				
Continent				
Europe	11	0.265 (0.195,0.341)	11.90 (<0.001)	97.761 % (<0.001)
South America	4	0.195 (0.053,0.396)	3.708 (<0.001)	97.630 % (<0.001)
Asia	15	0.357 (0.265,0.455)	11.825 (<0.001)	97.082 % (<0.001)
North America	11	0.295 (0.255,0.337)	23.727 (<0.001)	99.967 % (<0.001)
Africa	1	0.442 (0.335.0.553)	12.539 (<0.001)	N
Study type				
Cross-sectional	26	0.353 (0.273,0.437)	13.638 (<0.001)	98.923 % (<0.001)
Cohort	15	0.234 (0.203,0.267)	24.641 (<0.001)	99.940 % (<0.001)
Case-control	1	0.130 (0.071,0.212)	6.504 (<0.001)	N
Number of center				
Single-center	22	0.340 (0.260,0.425)	13.000 (<0.001)	96.534 % (<0.001)
Multi-center	20	0.250 (0.227,0.274)	36.374 (<0.001)	99.942 % (<0.001)
Location				
Hospital	35	0.306 (0.285,0.327)	47.577 (<0.001)	98.962 % (<0.001)
Community	7	0.232 (0.128,0.355)	6.818 (<0.001)	97.959 % (<0.001)
Diagnostic criteria of COPD				
GOLD	33	0.319 (0.260,0.381)	16.866 (<0.001)	97.393 % (<0.001)
Non-GOLD	9	0.235 (0.204,0.268)	25.203 (<0.001)	99.975 % (<0.001)
Diagnostic criteria of OSA				
PSG: AHI>5	12	0.385 (0.257,0.522)	8.959 (<0.001)	97.553 % (<0.001)
PSG: AHI>5 + related syndrome	3	0.266 (0.012.0.671)	2.341 (0.019)	N
PSG: AHI>10	2	0.252 (0.198,0.310)	14.743 (<0.001)	N
PSG: AHI>15	8	0.354 (0.258,0.457)	11.164 (<0.001)	95.239 % (<0.001)
Questionnaire	5	0.493 (0.353,0.633)	10.313 (<0.001)	96.761 % (<0.001)
Medical records or personal response	8	0.154 (0.104,0.211)	9.803 (<0.001)	92.548 % (<0.001)
ICD	4	0.143 (0.108,0.182)	14.381 (<0.001)	N
RLS				
Continent				
Asia	7	0.230 (0.159,0.308)	10.098 (<0.001)	85.572 % (<0.001)
Europe	2	0.253 (0.206,0.303)	17.164 (<0.001)	N
North and South America	3	0.142 (0.026,0.328)	3.160 (0.002)	N
Number of Center				
Single-center	8	0.259 (0.185,0.341)	10.794 (0.001)	86.046 % (<0.001)
Multi-center	4	0.139 (0.037,0.291)	3.745 (0.001)	N
Diagnostic criteria of COPD				
GOLD	8	0.257 (0.200,0.318)	14.311 (<0.001)	82.208 % (<0.001)
Non-GOLD	4	0.135 (0.029,0.299)	3.351 (<0.001)	97.865 % (<0.001)
Diagnostic criteria of RLS				
IRLSSG	8	0.278 (0.234,0.323)	20.257 (<0.001)	57.087 % (0.002)
Non-IRLSSG	3	0.108 (0.028,0.230)	3.650 (<0.001)	98.424 % (<0.001)
Insomnia				
Continent				
Asia	6	0.262 (0.120,0.434)	5.402 (<0.001)	98.6 % (<0.001)
Europe	3	0.235 (0.123,0.368)	6.357 (<0.001)	N
North America	3	0.413 (0.359,0.468)	23.498 (<0.001)	N
Number of centers				
Single-center	6	0.373 (0.234,0.524)	7.981 (<0.001)	
Multi-center	6	0.224 (0.073,0.426)	4.224 (<0.001)	99.365 % (<0.001)
Diagnostic criteria of COPD				
GOLD	8	0.273 (0.166,0.395)	7.769 (<0.001)	99.092 % (<0.001)
Non-GOLD	4	0.339 (0.228,0.459)	9.390 (<0.001)	95.101 % (<0.001)

GOLD: Global Initiative for Chronic Obstructive Lung Disease; PSG: Polysomnography; ICD: International Classification of Diseases; AHI: Apnea-Hypopnea Index; IRLSSG: International Restless Legs Syndrome Study Group.

RLS prevalence compared to other criteria, suggesting the widespread use of GOLD and IRLSSG criteria may help reduced the missed diagnostic rate of RLS. For insomnia, although we could not explain the heterogeneity of insomnia prevalence via sensitivity analysis, subgroup analysis and meta-regression, different diagnostic criteria, ethnicities and geographical locations may be responsible for the varied insomnia prevalence and heterogeneous results in our work.

There are still some limitations in our work that need to be discussed. First, the accurate prevalence of sleep disorders in the real world could not be obtained because some patients can be diagnosed with more than one kind of sleep disorder, and we can't extract such data from these articles. Second, although we conducted sensitivity analysis, subgroup analysis and meta-regression, we could only partly explain the source of heterogeneity. Third, we only included observational studies in English in this work, with diagnostic criteria of COPD and sleep disorders varied among eligible literature sources. Although we conducted subgroup analysis to verify the results, the risk of potential bias can not be ignored.

5. Conclusion

In conclusion, prevalence of OSA, RLS, and insomnia in COPD patients reached 29.1 %, 21.6 % and 29.5 %, respectively, which were higher than those in the overall population. OSA patients with COPD were characterized by a higher proportion of males, obesity, higher ESS scores, better pulmonary function and higher comorbidity risks, while COPD patients with RLS were associated with longer COPD duration and higher ESS scores. COPD patients with insomnia were characterized by female sex. Physicians need to be aware of sleep disorder evaluation and management in COPD patients. Further studies are needed to reveal the relationship between COPD and sleep disorders.

Ethical approval

Not applicable.

Consent to publish

Not applicable.

Table 3
Meta-regression for sleep disorders prevalence in COPD patients.

Variable	Coefficient	Standard error	T	Lower 95 % CI	Upper 95 % CI	P value
OSA						
Age	0.0001	0.007	0.02	−0.015	0.015	0.987
Proportion of male	−3.36e-07	2.70e-07	−1.24	−8.84e-07	2.12e-07	0.222
BMI	0.017	0.012	1.40	−0.008	0.041	0.174
Smoking(ever)	0.089	0.441	0.20	−0.872	1.05	0.844
Smoking(current)	0.207	0.288	0.72	−0.415	0.829	0.485
PaO2	−0.003	0.004	−0.85	−0.012	0.006	0.426
PaCO2	−0.002	0.006	−0.28	−0.014	0.012	0.786
FEV1%	0.010	0.005	2.09	−0.0001	0.02	0.052
FEV1/FVC	0.005	0.007	0.76	−0.009	0.02	0.462
ESS score	0.023	0.034	0.67	−0.06	0.106	0.670
Hypertension	−0.270	0.438	−0.62	−1.186	0.646	0.545
Diabetes mellitus	0.019	0.322	0.06	−0.663	0.701	0.953
Coronary disease	−1.048	1.165	−0.9	−3.898	1.802	0.403
Pulmonary hypertension	−0.876	1.11	−0.79	−5.652	3.899	0.513
Depression	1.464	0.303	4.83	0.623	2.305	0.008
CAT-T	−0.030	0.032	−0.93	−0.107	0.048	0.387
RLS						
Age	0.002	0.008	0.21	−0.017	0.021	0.841
Proportion of male	−0.194	0.321	−0.60	−0.933	0.545	0.562
BMI	−0.040	0.016	−2.52	−0.085	0.004	0.065
Smoking(packs/year)	0.004	0.002	1.63	−0.004	0.012	0.201
Insomnia						
Age	0.011	0.011	1.05	−0.013	0.035	0.326
Proportion of male	0.038	0.391	0.10	−0.846	0.922	0.925
BMI	0.036	0.054	0.67	−0.103	0.176	0.532
Smoking(ever)	−0.542	0.427	−1.27	−2.381	1.297	0.332
Smoking(current)	−0.746	0.965	−0.77	−3.425	1.933	0.483

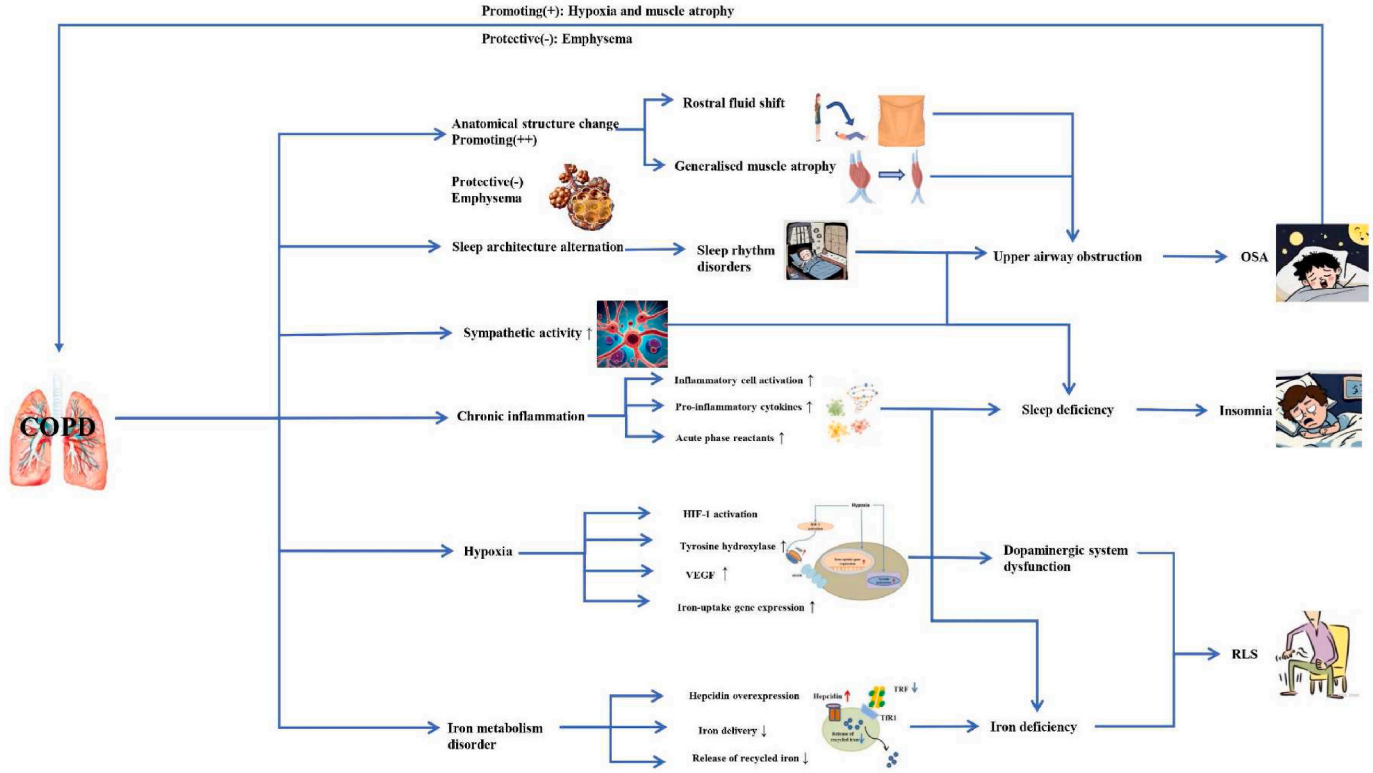

Fig. 3. Potential mechanisms of COPD's impact on OSA, RLS and insomnia. HIF-1: Hypoxia inducible factor-1 VEGF: Vascular endothelial growth factor.

Authors' contributions

YCS, DRD, XOL and FQW designed the study. DRD, GYZ, DX, LL, XRH and LC searched the literature and extracted available data. GYZ and DRD conducted statistical analysis. DRD wrote the manuscript. YCS and XOL revised the manuscript. All authors reviewed and approved the final manuscript. DRD and GYZ contributed equally to this work.

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Availability of data and materials

All data used and analyzed in this work are available from the corresponding author on reasonable request.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Abbreviations

OSA	Obstructive sleep apnea
RLS	Restless leg syndrome
COPD	Chronic obstructive pulmonary disease
CIs	Confidence intervals
ESS	Epworth sleepiness scale
YLLs	Year of life lost
AECOPD	Acute exacerbation of COPD
OR	Odds ratio
MD	Mean difference
BMI	Body mass index
FEV1%	Percentage of forced expiratory volume in 1 s
IRLSSG	International RLS Study Group
CRP	C-reactive protein
NLR	Neutrophil to lymphocyte ratio
TNF-α	Tumor necrosis factor-α
AHI	Apnea–Hypopnea index
HIF-1	Hypoxia inducible factor-1
VEGF	Vascular endothelial growth factor

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.sleep.2023.10.034.

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