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ORIGINAL RESEARCH

Association Between Sleep Quality and Pain Intensity in Mild Patients with COPD: A Community Study

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Qian Xu[1]
Kang Wu[2]
Yi Yang[2]
Rui Chang[1]
Hua Qiu[2]
Yingying Wang[1]
Tao Lin[2]
Chaowei Fu[1]
Yue Chen[3]
Na Wang[1]
Xiaonan Ruan[2]

[1]School of Public Health, Fudan University, Pudong Preventive Medicine Research Institute of Fudan University, Shanghai, 200032, People's Republic of China; [2]Pudong New Area Center for Disease Control and Prevention, Pudong Preventive Medicine Research Institute of Fudan University, Shanghai, 200136, People's Republic of China; [3]School of Epidemiology and Public Health, Faculty of Medicine, University of Ottawa, Ottawa, ON, Canada

Purpose: Poor sleep quality and pain were common and had been proved as an important influenced factor of quality of life for patients with COPD. The association of sleep quality with pain has been observed in other population but remains unclear in mild patients with COPD from a community setting.

Methods: A cross-sectional study was conducted to include eligible mild patients with COPD in Pudong New District of Shanghai. A structured questionnaire was used to collect general and clinical information for the patients. The Chinese version of Pittsburgh Sleep Quality Index (PSQI) and the short form of McGill Pain Questionnaire (SF-MPQ) was used to assess sleep quality and intensity of pain. Logistic regression was performed to test the association between sleeping quality and pain intensity.

Results: Two hundred and sixty-four patients with COPD, with an average age of 64 years (SD 5.78 years), were enrolled, and of 52% were women. Seventy-one (26.9%) participants reported at least one exacerbation during the past year. About 28.2% of the patients were classified as having poor sleep quality. Sleep quality was significantly associated with PRI score (adjusted odds ratio (ORad)=2.16, 95% CI: 1.16–4.00) and PPI rank (ORad=1.90, 95% CI: 1.08–3.34). People with daytime disturbance were more likely to have pain (ORad =2.03, 95% CI: 1.18–3.50).

Conclusion: Poor sleep quality was common in mild patients with COPD in community and was associated with higher pain intensity. Pain may involve an impairment of sleep quality.

Keywords: sleep, pain, chronic obstructive pulmonary disease, Pittsburgh sleep quality index, SF-MPQ

Introduction

Chronic obstructive pulmonary disease (COPD), characterized by persistent respiratory symptoms and airflow limitation, is a common disease and one of the leading causes of mortality in the world[1] and patients with COPD are frequently complicated by sleep disorders.[2,3] These sleep disorders and some nocturnal alterations in ventilation and symptoms, such as insomnia, cough and sputum[4–6] may cause difficulty initiating and maintaining sleep, with possible results of daytime sleepiness,[7] cognitive dysfunction,[8] changes of immune function,[9] even prone to acute exacerbations of COPD.[10]

Sleep quality, assessed by the Pittsburgh Sleep Quality Index (PSQI), has been commonly reported in patients with COPD and has been proved as an important predictor of quality of life in patients with COPD.[11–14] As a likewise common

Correspondence: Na Wang
School of Public Health, Fudan University, Pudong Preventive Medicine Research Institute of Fudan University, No. 130, Dongan Road, Xuhui District, Shanghai, 200032, People's Republic of China
Tel/Fax +86 21-54237455
Email na.wang@fudan.edu.cn

Xiaonan Ruan
Pudong New Area Center for Disease Control and Prevention, Shanghai, 200136, People's Republic of China
Tel/Fax +86 21-50342409
Email xnruan@pdcsc.sh.cn

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problem in COPD, pain, with a pooled prevalence of 66% in moderate and severe patients with COPD,[15] is associated with increased dyspnoea,[16] fatigue,[17] some specific comorbidities[16] and has been proved to decrease the quality of life in patients with COPD.[18] The impairment in pain and sleep can have a negative impact On health and well-being in patients with COPD. A pooled prevalence of 44% in co-occurrence of pain and sleep disturbance has been reported, in which 72% patients with chronic pain had insomnia.[19] This association between pain and sleep quality might be bidirectional.[20] The persistence and exacerbation of pain might cause the sleep disturbance.[21] Whereas disturbed sleep could change the resistance to pain[22] and non-disturbed sleep also might alleviate the pain as well.[23] Sleep quality and pain have common influence factors, such as anxiety and depression. Previous studies suggested that poor sleep quality was a predictor of negative emotion,[24,25] vice versa.[26] Similar bidirectional association was also observed between pain and negative emotion.[27]

This association of poor sleep quality with body pain has been usually observed in general population[28] as well as patients with lung cancer[29] and COPD,[30] but rarely in patients with mild COPD. According to a nationwide prevalence study in China, among adults with COPD, 56.4% had mild disease (GOLD 1) and only 7.4% had severe or very severe disease (GOLD 3 and GOLD 4).[31] Therefore, in this study, we investigated the relationship between sleep quality and pain intensity in patient with mild COPD, with a community setting, to provide epidemiological evidence for prevention and management of patients with mild COPD in China.

Materials and Methods

Study Population and Design

This was a cross-sectional study based on a community setting in Pudong New District of Shanghai, China, in the year of 2018. Ten communities were randomly selected from 46 communities in Pudong New District to recruit patients with mild patients in a register system established in 2014 including data of diagnosed COPD patients from local hospitals.[32]

The eligible subjects were included in this study only with the following criteria: (1) aged 40 years or older; (2) with mild (GOLD 1: forced expiratory volume in one second [FEV1]/forced vital capacity [FVC] <0.7 and FEV1 ≥80% predicted) COPD (verified by on-site spirometry during the survey); (3) local residents or lived in Pudong for more than two years; (4) willing and able to provide informed written consent, medical records and complete the survey (including questionnaire and spirometry) independently. Patients were excluded if they (1) were in severe or unstable medical conditions, such as cardiovascular, neurological, musculoskeletal diseases, and acute exacerbation (described by acute changes in respiratory symptoms) within one month; and/or (2) had cognitive impairment and mobility limitation. All included patients with COPD were previously diagnosed by physician and had a clam of COPD by Tenth Revision of International Classification of Disease codes related COPD: J43.x, and J44. x. All information was collected by using structured questionnaires in a face-to-face interview. Field investigators were trained together with a unified standard before the study was conducted and all questionnaires were double checked to ensure the accuracy and completeness of data. Finally, 264 out of 300 recruited mild patients with COPD fully completed the survey and submitted informed consents, with a response rate of 88.0%.

Measurements and Covariates

Spirometry

Spirometry was used to assess the severity of COPD among participants by measuring values of FEV1 and FVC as well as FEV1% predicted according to GOLD recommendation.[1] The lung function was tested 10 minutes after the short-acting beta2-agonist (Salbutamol Sulfate Solution for inhalation) was given. The ratio of FEV1 and FVC (FEV1/FVC) was calculated and compared with values of FEV1% predicted to help select mild patients with COPD in this study.

Sleep Quality

Sleep quality was assessed by the Chinese version of Pittsburgh Sleep Quality Index (PSQI), which has been validated and widely used.[33] In this questionnaire, information on 19 questions were collected to assess 7 domains of sleep quality: 1) perceived sleep quality, 2) sleep latency, 3) sleep duration, 4) sleep efficiency, 5) sleep disturbance, 6) use of sleep medication and 7) daytime dysfunction. Each domain of PSQI scored from 0 to 3, and then constituted a total PSQI score ranging from 0 to 21. A validated three-factor analysis was also used, which is favoured better than a single score in statistics[34] Factor 1, Sleep Efficiency, includes sleep duration and efficiency (score, 0–6). Factor 2, Sleep Quality, includes the

perceived sleep quality, sleep latency, and sleep medication use (score, 0–9). Factor 3, Daily Disturbances, includes sleep disturbances and daytime dysfunction (score, 0–6). A cut off of 7 was used to all participants categorized all patients into either the poor or good sleep quality group with a sensibility and specificity of 98.2% and 90.2%.[35] Specific categories were used to describe some sleep characteristics: long sleep latency (>30 vs ≤30 minutes), short sleep duration (<7 vs ≥7 hours), sleep medication use (≥once a week vs <once a week).

Pain Assessment

Pain severity was assessed by the short-form McGill Pain Questionnaire (SF-MPQ)[36] with satisfactory reliability and validity.[37] The SF-MPQ had three sections. 1) The pain rating index (PRI) was comprised of sensory subscale with 11 items and affective subscale with 4 items. Each item was scored from 0 (none) to 3 (severe). The total PRI score was obtained by summing scores of 15 items (range 0–45). 2) A 100-mm visual analogue scale (VAS) scored from 0 to 100 was used to rate the intensity of average pain. 3) Present pain intensity (PPI) with 5 scales from 0 (no pain) to 5 (extreme pain) was used to assess intensity of current pain.

Anxiety/Depression

Anxiety and depression were assessed by Chinese version of Hospital Anxiety and Depression Scale (HADS). HADS consists of 14 items, seven reflecting anxiety subscale (HADS Anxiety) and seven reflecting depression subscale (HADS depression).[38] Each item had a four-point (0–3) response. Hence, the total scores ranged from 0 to 21 for anxiety subscale and 0 to 21 for depression subscale. The cut-off value was recommended by 8–10 for doubtful cases and ≥11 for definite case.[39] A cut-off score of 8/9 for HADS was used with a sensibility and specificity of 93.7% and 72.6% for anxiety, and 84.6% and 90.3% for depression.[40]

Variables for Demographic and Clinical Information

During the interview, height and weight were measured and the body mass index (BMI) was calculated. Demographic information, including age, gender, retirement (retired vs unretired), education level (>9 vs ≤9 years), diagnosis date of COPD, self-reported exacerbation based on "symptom description" (during the past 12 months, no vs yes), history of common chronic diseases (physician diagnosed hypertension, cardiovascular diseases, type 2 diabetes, or chronic kidney disease), regular medicine use (self-reported and matched with recent medical records, yes vs no), were collected by using a structured questionnaire. Living habits such as ex/current smoker (≥1 cigarette a day for more than 6 months, yes vs no), self-reported second-hand smoke (exposure of more than 15 minutes a day, yes vs no), and exercise (any physical activities for more than 30 minutes, <once per week vs ≥once per week) were also collected in the questionnaire.

Statistical Analysis

All data were entered twice with Epidata 3.1 for double check. Considering the distribution of data, age was categorized by median (≤65 vs >65), while BMI was classified by WHO criteria (≤25 vs >25). Duration of COPD (<10 vs ≥10 years), numbers of self-reported comorbidity (0 vs 1 vs ≥2) were calculated and categorized. The scores of PSQI and pain intensity were presented by medium and interquartile ranges due to skewed distributions. However, to compare with previous research, the means of Skewed data were also mentioned in the text. The independent-samples *t*-test and $\chi 2$ test were used to compare variables between mild COPD patients with good and poor sleep.

To assess the association between sleep quality and pain intensity, logistic regression analysis was performed with PSQI category (>7 vs ≤7) as the primary outcome variable. Three confirmed factors were also performed by logistic regression as the secondary outcome, which were categorized by quartile (≤ low quartile vs >low quartile) Considering that the distributions of PPI, VAS, and total PRI scores were positively skewed, VAS and total PRI scores were regrouped into ≤median or >median and PPI rank into pain or no pain groups. The variables of Demographic information (eg, age, sex and BMI, retirement), clinical information (eg, exacerbation, numbers of comorbidities) and living habits (eg, smoking, exercise) were adjusted in the logistic regression analysis. We also performed the sensitivity analysis by excluding patients with anxiety or depression, to test the robustness of results. All the analysis were performed by SPSS (Version 22.0, IBM Corporation, New York, New York) as well. Two-sided P values less than 0.05 were considered statistically.

Ethics Approval and Informed Consent

All procedures performed in studies involving human participants were in accordance with the ethical standards of institutional research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. The Ethics Committee of Fudan University School of Public Health Institutional Review

Board approved this study (IRB#2016-07-0597). All participants provided written informed consent for participation. Informed consent was obtained from all individual participants included in the study. They were informed that all information collected in this study have been completely anonymized so that their identity cannot be identified via the paper.

Results

Of 300 eligible patients, 264 patients with mild COPD completed the survey, with a response rate of 88.0%. The average age of the 264 participants was 64 years (SD 5.78 years) and about 51.8% participants were female. Majority of patients (155/264, 58.7%) reported more than one comorbidity. The most common self-reported comorbidity was hypertension (43.2%,114/264), followed by cardiovascular diseases (14.0%, 37/264), type 2 diabetes (9.8%, 26/264) and others (5.7%,15/264). Of patients, 26.9% (71/264) reported having exacerbation in the past 12 months. Only 21% patients (58/263) were current smokers. The prevalence of anxiety and depression were 6.6% and 9.9%, respectively (Table 1).

Of patients with mild COPD, only 13.6% participants (36/264) reported problem to initiate sleep (sleep latency >30 minutes), 5.3% (14/264) used sleep medication and over 60% patients (166/264) had a sleep duration of no

Table 1 Characteristics of Study Population (N=264)

Characteristics	Total (N=264)
Gender, n (%)	
Male	128(48.5)
Female	136(51.5)
Age (years), n (%)	
≤65	139(52.7)
> 65	125(47.3)
BMI (kg/m2), n (%)	
< 25	139(52.7)
≥ 25	125(47.3)
Retirement, n (%)	
Unretired	155(58.7)
Retired	109(41.3)
Education (years), n (%)	
≤ 9	218(82.6)
> 9	46(17.4)
COPD duration (years), n (%)	
< 10	190(72.0)
≥ 10	74(28.0)
Exacerbation, n (%)	
Unhappened	193(73.1)
Happened	71(26.9)
Number of self-reported comorbidities, n (%)	
0	109(41.3)
1	111(42.0)
≥2	44(16.7)
Current smokers[a], n (%)	
No	209(79.5)
Yes	54(20.5)
Second-hand smokers[a], n (%)	
No	133(50.6)
Yes	130(49.4)
Exercise, n (%)	
< once per week	128(48.5)
≥ once per week	136(51.5)
Anxiety, n (%)	
HADS Anxiety<9	246(93.2)
HADS Anxiety ≥9	18(6.8)
Depression, n (%)	
HADS Depression<9	239(90.5)
HADS Depression ≥9	25(9.5)
Sleep Characteristics	
PSQI score, medium (IQR)	5.0(3.0, 8.0)
Poor sleepers (PSQI>7), n (%)	74(28.0)
Factor 1: Sleep efficiency, medium (IQR)	1.0(0.0, 3.0)
Factor 2: Sleep quality, medium (IQR)	2.0(1.0, 3.0)
Factor 3: daytime function, medium (QR)	2.0(1.0, 3.0)
Pain Characteristics	
PRI sensory dimension, medium (IQR)	0.0(0.0,1.0)
PRI affective dimension, medium (IQR)	0.0(0.0,2.0)
PRI total score, medium (IQR)	1.0(0.0, 3.0)
(> 0), n (%)	160(60.6)
VAS score[b], medium (IQR).	0.0(0.0, 1.0)
(> 0), n (%).	98(37.5)
PPI rank, n(%).	
No pain	164(62.1)
With pain (mild or above)	100(37.9)

Note: [a]1 case missing, [b]3 cases missing.

Abbreviations: BMI, body mass index; COPD, chronic obstructive pulmonary disease. PSQI: Pittsburgh Sleep Quality Index; PRI, pain rank index; PPI, present pain intensity; VAS, visual analogue scale; IQR, interquartile range.

less than 7 hours. As shown in Table 1, The median (IQR) PSQI score was 5.0 (3.0, 8.0) and the prevalence of poor sleepers (PSQI>7) was 28.2%. The median (IQR) of factor 1 (Sleep efficiency), factor 2 (Sleep quality) and factor 3 (daytime function) were 1.0 (0.0, 3.0), 2.0 (1.0, 3.0) and 2.0 (1.0, 3.0), respectively. The median scores of PRI and VAS were 1.0 (0.0, 3.0) and 0.0 (0.0, 10.0). Of all participants, 38.1% (104/264) reported pain by PPI rank. As shown in Table 2, of patients with poor sleep, 74.3% reported higher pain intensity by PRI and 48.6% had mild and above pain within 24 hours of the interview (PPI). Both PRI and PPI showed significant difference between patients with different sleep conditions and prompt that patients with poor sleep suffered from higher pain intensity.

Table 3 illustrated the results from multiple logistic regression analysis. COPD patients with higher pain intensity were more likely to have poor sleep quality. Compared with COPD patients without pain according to PPI, those with pain had a poorer sleep quality, with adjusted odds ratio (OR) of 1.90 (95% CI: 1.08–3.34). Similar results were observed when using PRI (OR_{ad}=2.16, 95% CI: 1.16–4.00).

The association of sleep factors with higher pain intensity according to PRI scores was only observed in daytime disturbance, with the adjusted odds ratio (OR) of 2.03 (95% CI:1.18–3.50) (Table 4). The association of sleep with pain intensity remained when participants with anxiety/depression were excluded, with the corresponding ORs for PRI, VAS, and PPI rank of 2.14 (95% CI:1.14 −4.02), 2.01 (95% CI:1.06–3.82), and 2.18 (95% CI:1.15–4.27) respectively.

Table 2 Sleep Quality and Pain Intensity in Patients with Mild COPD

	Good Sleepers (N=190)	Poor Sleepers (N=74)	*P* value
PRI scores, n(%)			
≤ 0	85(44.7)	19(25.7)	0.004
> 0	105(55.3)	55(74.3)	
VAS[a], n(%)			
≤ 0	124(66.0)	39(53.4)	0.061
> 0	64(34.0)	34(46.6)	
PPI rank, n(%)			
≤ 0 (No pain)	126(66.3)	38(51.4)	0.024
> 0 (With pain)	64(33.7)	36(48.6)	

Note: [a]3 case missing.
Abbreviations: PRI, pain rank index; PPI, present pain intensity; VAS, visual analogue scale.

Discussion

Although previous studies have investigated the relationship between sleep and pain in general population,[41,42] to our knowledge, this is the first study to assess the association of sleep quality with pain intensity in patients with mild COPD based on a community population. In our study, poor sleep quality was significantly associated with higher pain intensity in patients with mild COPD.

About 28% of our study patients had poor sleep (PSQI>7). Previous studies reported a higher prevalence of poor sleep quality of more than 50% in patients with COPD, especially in severe/very severe patients.[11,13,14] However, recent research in Asian patients with mild to moderate COPD by Lee, S. H. showed that 33.1% patients reported having a poor night sleep assessed by COPD and Asthma Sleep Impact Scale (CASIS),[43] which was slightly higher than that in our study. This difference in the severity of COPD patients might be the underlying cause. There were about 66% patients with moderate COPD in the research of Lee, S. H,[43] but all participants were mild patients with COPD in our research. The prevalence of pain assessed by PPI (PPI>0) was 38.1% and the intensity of pain assessed by SF-MPQ was the main influencing

Table 3 Association Between Sleep Quality (PSQI>7 Vs PSQI≤7) and Pain in Patients with Mild COPD

Variables	Adjusted Odds Ratio (95% CI)		
	Model 1	Model 2	Model 3
PRI Score, (>0 vs =0)	2.27(1.24–4.13)	2.22(1.21–4.07)	2.16(1.16–4.00)
VAS, (>0 vs =0)	1.66(0.95–2.91)	1.60(0.91–2.81)	1.61(0.90–2.87)
PPI Rank, (pain vs no pain)	1.81(1.04–3.15)	1.77(1.02–3.09)	1.90(1.08–3.34)

Notes: Model 1 adjusted for gender, age, BMI. Model 2 adjusted for exacerbation, numbers of comorbidity and covariates in model 1. Model 3 adjusted for retirement, smoking, exercises and covariates in model 2.
Abbreviations: PRI, pain rank index; PPI, present pain intensity; VAS, visual analogue scale; PSQI, Pittsburgh Sleep Quality Index; BMI, body mass index; COPD, chronic obstructive pulmonary disease.

Table 4 Association Between Different Sleep Factor with Pain in Patients with Mild COPD

Variables	Sleep Efficiency (>0 vs =0)	Sleep Quality (>0 vs =0)	Daytime Disturbance (>1 vs ≤1)
	Adjusted Odds Ratio (95% CI)	Adjusted Odds Ratio (95% CI)	Adjusted Odds Ratio (95% CI)
PRI Score, (>medium vs ≤medium)	1.04(0.62–1.75)	1.65(0.98–2.78)	2.03(1.18–3.50)
VAS, (>medium vs ≤medium)	1.20(0.71–2.04)	1.25(0.73–2.13)	1.08(0.61–1.89)
PPI Rank, (pain vs no pain)	1.22(0.71–2.02)	1.55(0.91–2.62)	1.46(0.71–3.04)

Note: Model adjusted for gender, age, BMI, exacerbation, numbers of comorbidity, retirement, smoking, exercises.
Abbreviations: PRI, pain rank index; PPI, present pain intensity; VAS, visual analogue scale; PSQI, Pittsburgh Sleep Quality Index; BMI, body mass index; COPD, chronic obstructive pulmonary disease.

factor to sleep in our research. A systematic review in patients with COPD revealed that the prevalence of pain ranged from 32 to 60%.[44] For those with mild COPD the prevalence of 37.9%, reported from the research of Tian Xiao, was close to our results.[45]

Our research found that different measures of pain including PRI score, VAS and PPI were associated with a higher risk for poor sleep quality in mild patients with COPD, which suggested that higher pain intensity in patients with COPD reduced their sleep quality. This result was similar to the finding from the previous researches. Among patients with COPD,[46] insomnia was independently associated with pain (β=0.71, p<0.05). Among patients with Parkinson's disease,[47] poor sleep quality was associated with different types of pain, like akathisic pain (OR: 4.69, p<0.001) and radiating pain (OR: 3.98, p<0.05). Among adolescents and young adults, higher levels of pain intensity were associated with higher PSQI scores (β = 0.23, p<0.001 and β=0.14, p< 0.01).[48] Similar association between poor sleep quality and increased pain was also observed among patients with stable heart failure.[49]

In addition to overall sleep quality assessed by total PSQI score, we also investigated the impact of pain on sleep efficiency, sleep quality and daytime disturbance respectively. No statistically significant association was observed between sleep efficiency/ quality and pain, which was consistent with some other studies. However, the relationship between shorter total sleep time and pain has been reported previously,[50,51] and their association might be bidirectional.[52] Use of sleep medication might contribute to reduce the interference from pain with sleep duration.[49] However, due to the low proportion of use of sleep medication, we failed to examine their association. Patients in our study had low scores of SF-MPQ and low intensity of pain, which might be inadequate to interrupt the sleep and interfere with sleep latency. Like previous studies in elder adults and patients in other chronic conditions, we found that pain was associated with daytime dysfunction, such as daytime sleepiness,[49] fatigue,[53] and increased napping.[54] However, PSQI merely contained two questions about daytime dysfunction. More detailed instruments and information about daytime dysfunction were necessary.

The biobehavioural mechanisms underlying the association between sleep and pain are not entirely clear. One hypothesis was related to inflammation. Previous studies found that both pain[55] and insomnia symptoms[56] were significantly associated with higher levels of inflammation biomarkers. Lower sleep duration was proved to increase the level in blood of C-reactive protein (CRP),[57] IL-6[58] and TNF-α.[59] These cytokines might result in histamine-induced vasodilation, causing the redness, swelling, pain, and warmth, which were characteristics of general pain.[60,61] Moreover, it has been found that negative mood plays an possible medium adjusting role in the association between sleep and pain in non-clinically depressed people.[62] Depression and anxiety are common comorbidities in patients with COPD as well,[63] which may partially explain the association between sleep quality and pain in this population. However, in the present research, only 12.9% patients had anxiety/depression problems. After excluding those patients with anxiety/depression, the association between sleep and pain remained significant.

The strength of our study mainly includes the use of reliable and validated scales for assessment of sleep quality and pain intensity, as well as recruitment of patients with COPD from community settings. There are also several limitations. First, as a cross-section study, we have to preclude the causal inference between sleep and pain. Secondly, SF-MPQ provides the assessment for the intensity of pain, but not for

a comprehensive understanding of pain. Further study should collect more clinical and non-clinical information on pain, such as pain extents and the impact of pain. Thirdly, although we assumed that daytime dysfunction was related with increased pain, more detailed and comprehensive instrument to evaluate this relationship in patients with mild COPD was needed. Moreover, the current analysis examined the association only in mild COPD patients, patients with other severity of COPD were not included.

Conclusion

Our study in community mild COPD patients found that poor sleep quality was associated with higher pain intensity and daytime disturbance might play a major role in this association. Further studies are needed to explore this association in patients with moderate/severe COPD.

Data Sharing Statement

The raw data required to reproduce these findings cannot be shared at this time as the data also forms part of an ongoing study.

Ethics Approval and Informed Consent

All procedures performed in studies involving human participants were in accordance with the ethical standards of institutional research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. The Ethics Committee of Fudan University School of Public Health Institutional Review Board approved this study (IRB#2016-07-0597). Informed consent was obtained from all individual participants included in the study. They were informed that all information collected in this study have been completely anonymized so that their identity cannot be identified via the paper.

Author Contributions

Q.X.: Data collection, Analysis and Writing; K.W, Y.Y, R.C, H.Q, Y.W and T.L: Data collection and Investigation; C.F, X.R and N.W: Conception and Design; Y.C and N.W: Revising. All authors made substantial contributions to conception and design, acquisition of data, or analysis and interpretation of data; took part in drafting the article or revising it critically for important intellectual content; agreed to submit to the current journal; gave approval of the final version to be published; and agree to be accountable for all aspects of the work.

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Disclosure

The authors declare that they have no conflicts of interest for this work.

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