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Sedentary behavior is associated with chronic obstructive pulmonary disease

A generalized propensity score-weighted analysis

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Abstract

Chronic obstructive pulmonary disease (COPD) is the fourth and third leading cause of death worldwide and in China, respectively. Sedentary behavior has been shown to increase the risk of respiratory disease, such as asthma. However, the relationship between sedentary behavior and COPD is unclear. This study aimed to investigate the association between sedentary behavior and COPD.

Data was extracted from the 2018 a large-scale cross-sectional study of Chronic Disease and Lifestyle Population Survey in Sichuan Province of China, in which sedentary behavior and chronic diseases were self-reported according to medical records. The association between sedentary behavior on risk of COPD was estimated using multivariable regression model in non-matching cohorts and generalized propensity score-weighted (GPSW)cohorts, respectively, controlling for potential confounders.

Individuals who remained sedentary for more than 7 hours per day were more likely to have COPD than the control group (<3 hours) both in conventional multivariate logistic regression analysis (OR = 2.020, 95%*CI*: 1.575–2.585, $P < .001$) and GPSW analysis (OR = 2.381, 95%*CI*: 1.778–3.188, $P < .001$). After GPSW and the sensitivity analysis using refined smoking variable further found a dose-effect between sedentary behavior and COPD, with 1.242 (95%*CI*: 1.006–1.532, $P < .05$) times risk of COPD in those sedentary behavior of more than 5 hours per day (GPSW) and 1.377 (95%*CI*: 1.092–1.736, $P < .05$) times risk in those sedentary behavior above 5 hours per day (sensitivity analysis), comparing with the control group.

Sedentary behavior is independently associated with increased risk of COPD, adjusting for other confounders. The findings of this study have important implications for future research and public health guidance. Reducing sedentary time may have a significant role in COPD prevention.

Abbreviations: COPD = chronic obstructive pulmonary disease, GPS = generalized propensity score, GPSW = generalized propensity score-weighted, SMD = standardized mean differences.

Keywords: chronic obstructive pulmonary disease, generalized propensity score-weighted, inverse-probability weighted, sedentary behavior

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1. Introduction

Chronic obstructive pulmonary disease (COPD) is a major challenge for public health. According to the 2017 Global Burden of Disease Study (GBD), COPD is the 4th leading cause of death worldwide,[1] and the disease burden is higher in low-and middle-income countries.[2] In China, the prevalence of COPD is high and rising, being the third leading cause of death and loss of disability adjusted life years (DALYs).[3–5]

Recent research shows that sedentary behavior is a novel, important, and highly prevalent risk factor of chronic diseases.[6–8] However, research on the relationship between sedentary behavior and COPD remains scarce. Existing ones mainly focus on impacts of sedentary behavior in patients with COPD.[9–13] It was found that adhering to physical activity guidelines and keeping leisure-based sitting time reduced the odds of diabetes in people with COPD.[10] Physical activity and sedentary time may be predictors of healthcare use and quality of life in individuals with COPD.[11] Prospective study results suggested that sedentary behavior was an independent predictor of mortality in subjects with COPD,[12] adjusting for moderate to vigorous physical activity and a number of other variables.[13]

However, the association between sedentary time and the risk of COPD is unclear. The objective of this study was to explore the relationship between sedentary behavior and COPD.

2. Materials and methods

2.1. Data source

Data were extracted from a large epidemiological survey of the health status and influencing factors among residents in Sichuan Province of China in 2018 involving 14,290 participants. The survey was conducted face-to-face by trained community health workers. Multistage stratified cluster sampling method was used, including 3 metropolises (Chengdu, Ya'an, and Guangyuan), 6 counties (Dujiangyan county and High-tech zone in Chengdu, Shimian county in Ya'an, Qingchuan county in Guangyuan), 5 to 10 communities or townships of each county or district, 100 to 800 families of each community or township, and an adult over 18 years old in each family.

2.2. Exposure

Sedentary behavior was the exposure factor, which was classified according to its time per day. In the survey, participants were asked about the total time spending on (minutes a day) sitting or lying, including at work, at home, travel, sitting with friends, traveling by car, bus or train, reading books, playing cards, playing computer or watching TV, but not time on sleep.

All participants were classified into 4 groups by time of sedentary behavior per day as the follows: >7 hours per day (code 1), between 5 and 7 hours per day (code 2), between 3 and 5 hours per day (code 3), and <3 hours per day (code 4, as control group). Because previous studies showed that the sedentary behavior of more than 3 hours per day was related to adverse health consequences, though the specific time threshold for adverse health consequences over 3 hours was still uncertain.[14] And it was suspected that there might be a dose-effect between sedentary time and COPD.

2.3. Covariates

Covariates included gender, age, ethnicity, occupation, educational level, marital status, economic status, other chronic diseases, smoke, and physical activity.

Sex was classified into 2 groups (male and female); age was classified into 4 groups (18–34 years old, 35–49 years old, 50–64 years old, ≥65 years old); ethnicity was classified into 2 groups (Han ethnicity, others); occupation was classified into 5 groups (staff of state agencies, enterprises and institutions, farmers, other occupations, retired personnel, unemployed); education level was divided into 4 groups (primary school and below, junior high school, high school/technical secondary school/technical school, bachelor/college degree or above); marital status was divided into 4 groups (unmarried, married, divorce/separation, widowed); the economic situation was divided into 4 groups (low (monthly income below 4,000 RMB), middle [monthly income between 4000 RMB and 10,000 RMB), high (family monthly income above 10,000 RMB), and unclear]; other comorbidities of chronic diseases were classified into 2 groups (no, yes); smoke was classified into 3 groups (never smoke, smoking cessation, and current smoking).

Physical activity was measured in 3 aspects: working time, housework time, and leisure time, using Global Physical Activity Questionnaire (GPAQ).[15] One minute of strenuous exercise was deemed to be 2 minutes of moderate exercise. Then, the sum of strenuous and moderate physical activity was combined and measured as moderate physical activity. According to the definition of physical activity level in the International Physical Activity Questionnaire (IPAQ),[16] physical activity was divided into 2 groups: <150 minutes/week (under-activity); ≥150 minutes/week (enough-activity).

2.4. Outcome

The outcome of interest in this study was COPD. It was recorded as Yes in the questionnaire if participants responded that they had been diagnosed (confirmed through medical means) with COPD.

2.5. Statistical analysis

Two methods were used to adjust for potential confounders of outcome in this study: conventional multivariate logistic regression analysis and generalized propensity score weighted analysis (GPSW).[17]

2.5.1. Conventional Multivariate Logistic Regression Model. First, multivariate logistic analysis was used to examine the odds of COPD between sedentary behavior groups, adjusting for confounding factors of gender, age, nation, occupation, educational level, marital status, economic status, other chronic diseases, smoke, and physical activity.[18]

2.5.2. Generalized propensity score-weighted analysis. Generalized propensity score weighted (GPSW) analysis was conducted. Inverse propensity score weighting (IPSW) with the GPS estimated via generalized boosted model can be implemented using those scores to estimate weights and causal effects, which retains all patients' data and is stronger in reducing bias than stratification and covariate adjustment.[17] Generalized propensity score (GPS) was defined as the conditional probability of receiving a particular treatment given the pretreatment covariates, which facilitates the construction of data sets with

similar distributions of the covariates.[19] And it could address limitations of confounding bias, classification bias, and failure to abide by the intention to treat principle.[20]

A generalized boosted model was fitted, with levels of sedentary behavior exposure as outcome to estimate the GPS (sedentary behavior less than 3 hours per day as a control group). Because the aim of the GPS model was to obtain the best estimate of the probability of exposure assignment, over-parameterization was not a concern: 10 baseline covariates related to type of the sedentary behavior exposure or COPD outcomes were included in the model including sex, age, ethnicity, occupation, educational level, marital status, economic status, other chronic diseases, smoke, and physical activity.

Based on the obtained GPS, the inverse-probability-of-treatment weighted method is adopted to weight observations, which created potential sample (pseudo-population) for each exposure level t that are intended to represent the samples we would have observed if everyone had been received exposure t. We normalize the weights so that they add up to 1 in each exposure group.[21]

Standardized mean differences (SMD) were used to test the equilibrium of covariates after weighted.[18] It is generally believed that when the absolute value of the SMD was less than 0.1, the covariates between the 2 groups reached equilibrium. Since our study tested the covariance equilibrium among multiple groups, the maximum SMD between different groups was used as the test index.[22] Finally, binary logistic regression using GPSW data was conducted to estimate the association between sedentary behavior and the risk of COPD.

2.5.3. Sensitivity analysis. In survey data collected in Dujiangyan county, smoking behavior was recorded as binary variable (not smoking or smoking), and did not label people who quit smoking as that in other study cites (counties) later. To examine the impact of different classification of smoking variables on the results, the estimation of the effects of sedentary behavior on risk of COPD was performed using multivariate regression model by removing the data of Dujiangyan county.

Data analyses were performed using IBM SPSS Statistics version 25 (SPSS Inc., IBM, Chicago, Illinois, USA) and R version 4.0.2. When $P<.05$(bilateral), the results were considered as significant.

2.6. Ethical issues

The study protocol was approved by the Ethics Committee of West China School of Public Health (West China Fourth Hospital) of Sichuan University. All participants provided written informed consent before participating in the survey.

3. Results

3.1. Characteristics of participants and generalized propensity score-weighted

A total of 14,290 questionnaires were distributed to people over the age of 18 in the survey, with an effective rate of 98.48%. Finally, 14,073 adults (5488 males, 8585 females, with an average age of 53.1 ± 15.7 years old) were included in the analysis. Among the extracted participants, 749 individuals were identified as having COPD.

And the SMD of all covariates were less than 0.1 after weighted, indicating that selection bias of the known covariates was controlled by the weighted method. (Table 1)

3.2. Association between sedentary behavior and chronic obstructive pulmonary disease

The association between sedentary behavior and COPD estimated using conventional multivariate logistic regression (model 1) and GPSW (model 2) were presented in Figure 1. Individuals who remained sedentary for more than 7 hours per day were more likely to have COPD than those in the control group (<3 hours) both in model 1 (OR = 2.020, 95%CI:1.575–2.585, and $P<.001$) and model 2 (OR = 2.381, 95%CI:1.778–3.188, and $P<.001$). And individuals who remained sedentary between 5 and 7 hours per day also had a 1.242-fold (95% *CI*:1.006–1.532, and $P<.05$) higher risk of COPD than those sat less than 3 hours per day in model 2. (Figure 1)

3.3. Sensitivity analysis

The data of participants from Dujiangyan county which did not distinguish smoking cessation and never smoking (N = 2680) were excluded. There was an increased risk of COPD with incremental time of sedentary behavior. Comparing with participants with the sedentary behavior of less than 3 hours per day, there was 1.377 (95%CI:1.092–1.736, and $P<.05$) times risk of COPD in those had a sedentary behavior of more than 5 hours per day and 2.438 times (95% *CI*:1.831–3.247, and $P<.001$) risk of the participants whose sedentary behavior above 7 hours per day. (Table 2)

4. Discussion

The main finding of this study was that sedentary behavior was significantly associated with increased risk of COPD, controlling for other factors in both multivariate regression analysis and GPSM analysis. Individuals who sat more than 7 hours per day had a 2.02-fold higher risk of COPD than those sat less than 3 hours per day. After GPSW analysis and the sensitivity analysis which using better defined smoking variable further supported the association between sedentary behavior and COPD, not only with a stronger effect, but also dose-effect. Consistent with previous results,[23,24] in multiple logistic regression analysis, which results could be seen in annexed table 1, http://links.lww.com/MD/F996, older age, history of smoking (both current and former) were significant predictors of COPD. Sex-related differences regarding to COPD may be affected by other background factors.[25] The results from the study showed that males were more likely to have COPD than females, which was in agreement with the results of a meta-analysis.[24] Participants who had Other comorbidities of chronic diseases had a 1.904-fold higher risk of COPD than those not. Study before showed that chronic comorbidities are highly prevalent in primary care COPD patients, several chronic comorbidities were associated with having frequent exacerbations and increased exacerbation risk.[26] This may be related to the long-term use of drugs in COPD patients, for example, theophylline has many interactions with other drugs and which will have an impact on gastrointestinal tract, center, and cardiovascular system.[27]

The results of our study suggested that sedentary behavior may be an independent risk factor for COPD. There have been few

Table 1

Comparison of the mean percentage of baseline characteristics between research groups and control group.

Characteristic	First group (N = 4980)	Second group (N = 4788)	Third group (N = 3168)	Fourth group (N = 1137)	MSMD	
					Un-weighted	Weighted
Sex					0.077	0.039
Male	38.4	41.0	37.2	37.9		
Female	61.6	59.0	62.8	62.1		
Age					0.188	0.032
≥65 years old	23.9	26.2	30.1	27.2		
50–64 years old	30.7	34.5	32.5	28.8		
35–49 years old	29.4	27.0	23.3	25.7		
18–34 years old	16.0	12.3	14.1	18.3		
Ethnicity					0.079	0.007
Han nationality	89.6	89.0	91.4	90.1		
Others	10.4	11.0	8.6	9.9		
Education Level					0.344	0.027
Primary school and below	51.9	56.6	48.2	44.6		
Junior high school	21.8	25.0	25.1	22.7		
High school/Technical secondary school/Technical school	9.9	8.6	11.6	12.6		
Bachelor/College Degree or Above	16.4	9.8	15.1	20.1		
Marital Status					0.158	0.043
Unmarried	6.0	4.8	5.5	6.8		
Divorce/Separation/Widowed	11.1	10.2	12.5	14.2		
Married	82.9	85.0	82.0	79.0		
Occupation					0.572	0.027
Staff of state agencies, enterprises and institutions	19.8	10.8	15.8	19.4		
Farmer	61.6	64.9	43.9	38.3		
Other occupations	9.8	11.7	12.6	17.9		
Retired personnel	5.2	8.6	20.1	13.8		
Unemployed	3.6	4.0	7.6	10.6		
Economic Status					0.240	0.060
Low	81.4	81.3	77.8	72.7		
Middle	12.4	14.2	18.1	21.2		
High	0.9	0.7	0.5	1.4		
Unclear	5.3	3.8	3.6	4.7		
Other comorbidities of chronic diseases					0.359	0.023
No	75.2	68.0	65.5	58.6		
Yes	24.8	32.0	34.5	41.4		
Smoke					0.227	0.051
Never smoke	54.2	65.1	64.3	64.2		
Smoking cessation	7.7	5.2	6.3	5.7		
Current smoking	38.1	29.7	29.4	30.1		
Physical activity					0.343	0.015
Enough-activity	40.7	44.5	51.8	35.0		
Under-activity	59.3	55.5	48.2	65.0		

*First group: sedentary behavior below 3 hours per day; Second group: sedentary behavior between 3and 5 hours per day; Third group: sedentary behavior between 5 and 7 hours per day; Fourth group: sedentary behavior above 7 hours per day.

MSMD: The maximum standardized mean difference between different groups was used as the test index.

relevant studies. But our findings were supported by evidence from previous studies. It is evident that sedentary behavior was associated with less efficient pulmonary function.[28] Study also found that respiratory patterns are associated with sedentary activities, such as spontaneous sigh rates,[29] was important in regulation of airway smooth muscle tone and consequently airway responsiveness.[30] At present, the diagnosis of acute exacerbations of COPD is mainly dependent on clinical manifestations and lacks quantitative indicators. Quantitative indicator such as inflammatory biomarkers can assist more accurate diagnosis of acute exacerbations of COPD, among which C-reactive protein, serum amyloid A, serum alveolar surfactant protein-D are all commonly used inflammatory markers now.[31–33] There is a (positive) correlation between bacteria isolated from COPD deterioration and impaired lung function. Enterobacteriaceae is the main bacteria with aggravated illness.[34] Airway inflammation aggravates will cause bronchial mucosa congestion and edema, mucus secretion increased, smooth muscle spasm, and aggravate airway stenosis.[35] Longitudinal studies could be conducted in the future to explore the changes in inflammation markers in people with different sedentary conditions, to further elucidate the association between sedentary behavior and COPD from the biological mechanism perspective.

Asthma has been recognized as a risk factor for developing COPD. Comparing with non-asthmatics, active asthmatics had a 10-times-higher risk for acquiring symptoms of chronic bronchitis,[36] and sedentary time was an independent but modifiable

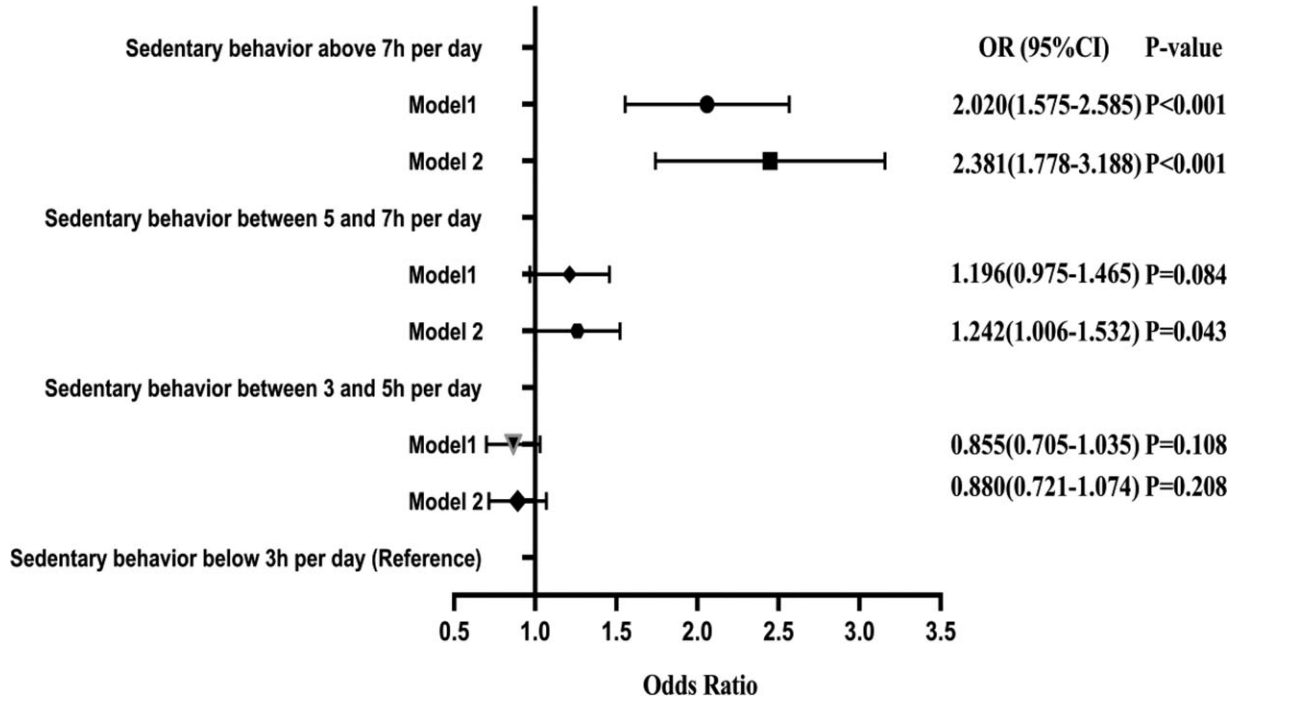

Figure 1. The effect of sedentary behavior on chronic obstructive pulmonary disease. The horizontal axis scale of the invalid line vertical line is 1, and each line is the line between the upper and lower limits of the 95% confidence interval of the study, which length visually represents the size of the confidence interval. The small figure in the center of the line is the position of the OR value, and its square size is the weight of the study. If the line of a study's 95% confidence interval straddles an invalid vertical line, the study is not statistically significant; conversely, if the horizontal line falls to the left or right of the invalid vertical line, the study is statistically significant.

factor of asthma.[37] Therefore, there might be a link between sedentary behavior and COPD through asthma, which warrants further investigation.

We also speculate that smoking may be a confounder of the association of sedentary behavior and COPD. Smoking, which had been proven in before studies, was a single most important risk factor for COPD.[38] Men smoke 3 times as much as women, and smoking consumption increases with age.[39] The results of sensitivity analysis in our study, which using a refined smoking variable, showed that there was a dose-effect association between sedentary behavior and COPD. However, the relationship between sedentary behavior and smoking are less conclusive[40] Future research may be necessary to explore the relationship between sedentary behavior and smoking.

Our study had several strengths. As far as we know, this is the first study to assess the association between overall sedentary behavior, rather than physical activity or a certain single sedentary activity, and COPD in southwest China. What is more, cross-validating the effects of sedentary behavior on COPD, using a traditional covariate controlling method (multivariate logistic regression model), GPSW methods with covariate adjustment, and sensitivity analysis. The results are stable and consistent, and show a dose-effect relationship, which enhances the credibility of the results.

However, there were several limitations in this study. First, since this was a cross-sectional study and data were collected retrospectively, the causal effect cannot be established. Further longitudinal study is needed to verify the causal-effect. Second, this study was based in Chinese population, further prospective investigations in other populations are needed. Third, the sedentary behavior in our study was based on self-reported data of respondents, and recall bias may be introduced. Future research should use objective measures of sedentary behavior that access for valid and reliable daily sedentary time. Fourth, COPD was defined as Yes in the questionnaire if participants answered that they had been diagnosed (confirmed through medical means) with COPD, however, some research indicates that under- and overdiagnosis of COPD remains a prevalent challenge.[41] Further study should explore the recognized and effective case-finding methods. Finally, smoking was adjusted as categorical variable in the model, more accurate estimation of the association between sedative behavior and COPD could be obtained if dose-effect of smoking is adjusted in future studies.

Table 2

Sensitivity analysis of the association between sedentary behavior and chronic obstructive pulmonary disease after excluding the first round data from Dujiangyan county.

Sedentary behavior	OR	95% *CI*	*P* value
Above 7 hours per day	2.438	1.831–3.247	<.001
Between 5 and 7 hours per day	1.377	1.092–1.736	.007
Between 3 and 5 hours per day	0.918	0.739–1.140	.438
Below 3 hours (control) per day			

*Analyses were adjusted for sex, age, nation, educational level, marital status, occupation, economic status, smoke, physical activity, and for all others chronic diseases.

5. Conclusion

In conclusion, there is preliminary evidence that sedentary behavior increases the risk of COPD compared with individuals who sit less. The findings of this study have important implications for future research and public health guidance. Reducing sedentary time may have a significant role in COPD

prevention. There is an urgent need to further investigate the impact of reducing sedentary time on COPD health.

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