Sleep Duration and Efficiency Associated With Better Functional Exercise Capacity in Black Smokers at Risk for COPD

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BACKGROUND: Black smokers have earlier development of lung disease as well as poorer sleep health than whites.

RESEARCH QUESTION: In a sample of black smokers, to what extent does sleep health modify the association between smoking level and functional exercise capacity?

DESIGN AND METHODS: Cross-sectional data from 209 black smokers (≥ 1 cigarette in last month), aged 40 to 65 years with no evidence of sleep-disordered breathing (apnea-hypopnea index < 15) or severe COPD ($FEV_1 > 50\%$), were used for the current study. Self-reported smoking rate, objectively measured sleep efficiency (SE), total sleep time (TST), and the 6-min walk test (6MWT) for functional exercise capacity were the key assessments.

RESULTS: The mean age was 54.8 years (SD, 5.96), and mean cigarettes smoked per day (cpd) was 8.71 (SD, 6.78). Mean SE was 69.9% (SD, 12.3%), and mean TST was 307.99 min (SD 92.2). In adjusted linear regression models of the 6MWT (meters), TST (slope estimate, -0.14 ; $P = .14$) and SE (slope estimate, -1.0 ; $P = .19$) were negatively associated with 6MWT. The smoking rate $\times$ SE interaction was highly significant (slope estimate, 0.18 ; $P = .007$) such that in individuals who smoked ≥ 10 cpd, every additional percentage of SE garnered an additional distance of 0.83 to 6.62 m. Similarly, the smoking rate $\times$ TST interaction was significant (slope estimate, 0.019 ; $P = .03$) such that in smokers who smoked ≥ 10 cpd, every additional minute of TST garnered an additional distance of 0.04 to 0.60 m.

INTERPRETATION: Higher SE and, to a lesser extent, longer TST, in black adults who smoke ≥ 10 cpd is associated with better 6MWT performance.

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KEY WORDS: 6-min walk test; black adults; sleep health; smoking

ABBREVIATIONS: AHI = apnea-hypopnea index; cpd = cigarettes per day; FEV_1/FVC = ratio between FEV_1 and FVC; SE = sleep efficiency; TST = total sleep time

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COPD is a progressive, debilitating respiratory condition that is the third leading cause of death among American adults.¹ Considerable racial disparity exists in the incidence, comorbidities, and mortality experienced from COPD. As compared with whites, black adults disproportionately account for the increase in COPD incidence over the last decade.^{2,3} Moreover, AA adults develop COPD at a younger age and with less intense smoking habits than non-Hispanic whites.⁴⁻⁶ Once diagnosed with COPD, AAs experience more severe symptoms,⁷ faster progression of disease, and greater declines in quality of life than whites.⁸⁻¹⁰ AAs with COPD also have higher rates of comorbidities including hypertension, stroke, and diabetes compared with whites, Asians, and Hispanics with COPD.¹¹

Sleep health may be a contributing factor to the lung and cardiovascular health disparity experienced by AA smokers. Sleep health as a concept is related to, but distinct from, clinical sleep disorders.¹² Sleep disorders pertain to the etiology, pathophysiology, and treatment of conditions such as sleep apnea, whereas sleep health encompasses metrics such as sleep efficiency and

duration.¹² Insufficient sleep duration (≤ 6 h) has been associated with a higher risk of exacerbations in smoking-related COPD,¹³⁻¹⁵ as well as several cardiovascular diseases including myocardial infarction and stroke,¹⁶⁻²⁰ independent of derangements in traditional metabolic mediators.²¹ Critically, AAs are less likely to get adequate sleep (7-8 h/night)²²⁻²⁸ and have lower sleep efficiency^{28,29} than whites. Tobacco use by itself has negative effects on sleep health³⁰ as demonstrated by the shorter sleep duration,^{31,32} and lower sleep efficiency³³ in smokers vs nonsmokers. Thus, the lung and cardiovascular health disparity experienced by AA smokers may be at least partially explained by poorer sleep health.

To add to our understanding of the role of sleep health in the etiology of cardiopulmonary-related diseases, we tested the hypothesis that among AA smokers, the cigarette smoking rate would be significantly and negatively associated with exercise capacity, but that this association would be mitigated in AA smokers with longer sleep duration and higher sleep efficiency.

Patients and Methods

Study Design and Population

This study was part of the ongoing Temple Lung Health Cohort Study, the aim of which is to quantify the extent to which sleep health relates to lung function in AA smokers. Participants are AA adults, aged 40 to 65 years, who smoke ≥ 1 cigarette in the last month, and are prodromal or have early-stage lung disease (ie, Global Initiative for Chronic Obstructive Lung Disease stage 0-2: $FEV_1 \geq 50\%$ of predicted).³⁴ $FEV_1 \geq 50\%$ of predicted was chosen as more severe degrees of airflow obstruction have been associated with increased mortality.³⁵ Likewise, apnea-hypopnea indexes (AHIs) of 0 to 15 events/h were included in the study given the unclear impact of mild OSA on daytime symptoms, cardiovascular risk, and the universal need for therapy.^{36,37} Individuals who had moderate-severe sleep apnea ($AHI \geq 15$ events/h) and who reported being pregnant (female), who used any form of sleep aid, or who had a history of lung cancer were ineligible.

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Screening and Recruitment

Patients were recruited from Temple University Hospital clinical waiting rooms by research staff and via local media (ie, radio) advertisements. Eligibility screening was conducted in three stages. Stage 1 assessed race, age, sex, smoking status, history of lung cancer, pregnancy, and sleep medication use. Of the 436 who completed this stage of screening, 30 were ineligible. Individuals meeting these criteria progressed to stage 2, where written informed consent was obtained followed by spirometric assessment of lung function (Vmax Encore PFT system, version 27-3; Vyair Medical), and carbon monoxide verification of smoking status (carbon monoxide ≥ 5 ppm). Spirometric values were derived from prebronchodilator testing, a practice that has been shown to maintain, after bronchodilator administration, the prognostic value of spirometry in COPD cohorts.^{35,38} Of the 384 AA smokers who completed this stage of screening, 20 were ineligible.

Consenting and initially eligible individuals then completed a one-night at-home sleep test to assess for OSA (stage 3). If the estimated AHI was ≥ 15 events/h (ie, moderate/severe OSA), individuals were excluded. Of the 364 who completed this stage of screening, 108 were ineligible, and 25 did not have a valid assessment. Of the 231 who were eligible, 22 were unreachable. Thus, the current study examines baseline data from 209 consenting and eligible participants. The study was approved by the Western Institutional Review Board (WIRB#: 20180370), and is registered at [ClinicalTrials.gov](https://clinicaltrials.gov).³⁹ The study consent form is available in e-Appendix 1 in the online article.

Data Collection and Measures

Study assessments were completed during a 2.5-h visit by a trained research technician.

The independent variable of interest was the self-reported smoking rate as indicated as cigarettes smoked per day (cpd), which was collected as part

of the Fagerström Test for Cigarette Dependence. Self-reported cpd is highly correlated with biochemical indicators of smoking status (eg, cotinine).⁴⁰

The dependent variable of functional exercise capacity was assessed on the basis of the 6-min walk test (6MWT).⁴¹ The 6MWT was conducted indoors according to the standardized protocol.⁴¹ During testing, heart rate and oxygen saturation were monitored with Rainbow SET pulse oximeters (Masimo). Heart rate was recorded at rest after sitting quietly for 1 min (1-min recovery heart rate).

The sleep health metrics of total sleep time (TST) and sleep efficiency (SE; the percentage of time in bed, asleep) were the study moderators of interest. TST and SE were captured with the Food and Drug Administration-approved, type III WatchPAT device (Itamar Medical), which uses finger-based physiology to assess sleep continuity and sleep architecture. The WatchPAT has a 90% concordance with polysomnography.⁴²

Study covariates included demographics (birth sex, educational attainment,⁷ BMI [kg/m²]), lung function, and medication use. Lung function was assessed by spirometry (Vitalograph ALPHA; Vitalograph Ltd). The key metrics of interest were the FVC and FEV₁ (volume delivered in the first second of an FVC maneuver) and the FEV₁/FVC ratio.⁴³ Current medication use was ascertained from medical records and coded as yes/no for the following categories: antihypertensives, nodal blocker agents, antidepressants, statins, long-acting bronchodilators, and diabetes medications. Use of these medications has been associated with exercise capacity.^{44,45} Depressive and lung disease symptoms were also assessed. Depressive symptoms was measured with the 20-item Center for Epidemiologic Studies-Depression (CES-D) Scale.⁴⁶ Lung disease symptoms were assessed with the Modified Medical Research Council (mMRC) test and the COPD Assessment Test (CAT). The mMRC asks participants to rate their degree of breathlessness on a scale of 0 to 4, where 0 indicates no breathlessness and 4 represents extreme breathlessness.⁴⁷⁻⁴⁹ The CAT provides a score of 0 to 40 to indicate the severity of lung impairment symptoms.⁵⁰

Results

Sample Characteristics

The analytical sample was composed of 209 adults and sample characteristics can be found in [Figure 1](#). The mean age was 54.75 ± 5.96 years and 58.8% were female (n = 123). Mean cpd was 8.71 ± 6.78. Mean SE was 69.9% (SD, 12.3), and mean TST was 307.99 min (SD, 92.2; ie, 5 h and 8 min). The mean 6MWT distance was 346.62 ± 78.24 m and the heart rate at 1 min of recovery was 88.16 ± 13.37 bpm. Simple bivariate associations with 6MWT distance are shown in [Table 1](#).

Moderating Effects of TST on the Association Between Smoking Rate and 6MWT Distance

In the fully adjusted multivariable linear regression model of the 6MWT, the smoking rate was significantly and negatively associated with 6MWT distance. Specifically, for each additional cigarette, the 6MWT distance covered was expected to decline by 5.37 m (slope estimate, -5.37; *P* = .04) ([Table 2](#)). The

Statistical Analysis

To generate the analytical sample, individuals with missing values for the 6MWT were excluded from analysis; those with missing values for any other modeling variables had such values imputed, using either logistic regression (binary variables) or predictive mean matching (continuous variables). Descriptive statistics were then generated for all study variables: mean and SDs for continuous variables, count and percentages for categorical variables. Bivariate associations between each study variable and 6MWT distance were estimated, using separate simple linear regression models. To assess moderating effects of sleep health metrics on the association between smoking rate and functional exercise capacity, a separate multivariable linear regression model was estimated for TST and SE; each model included an interaction term with the self-reported smoking rate. Both models adjusted for all covariates. Model assumptions were assessed using plots of residuals vs fitted values (linearity), the Breusch-Pagan test (homoscedasticity), variance inflation factors (no multicollinearity), and Q-Q plots (normality of residuals). Estimates of 6MWT distance change per additional 1% (SE) or 1 min (TST) were obtained as follows: first, the model-estimated contribution to 6MWT distance from TST/SE, a fixed daily smoking rate, and their interaction was computed. Next, the same value was computed, but a value of 1 was added to TST/SE. Finally, the “TST/SE” 6MWT distance was subtracted from the “TST/SE + 1” 6MWT distance. A general formula is provided below:

$$[x\beta_r + (y + 1)\beta_s + x(y + 1)\beta_{r \times s}] - (x\beta_r + y\beta_s + xy\beta_{r \times s})$$

$$[x\beta_r + y\beta_s + xy\beta_{r \times s}] = \beta_s + x\beta_{r \times s}$$

where *x* is the smoking rate, *y* is TST/SE, β_r is the model parameter estimate for the smoking rate, β_s is the model parameter estimate for TST/SE, and $\beta_{r \times s}$ is the model parameter estimate for the interaction between TST/SE and the smoking rate. Statistical significance was ascertained at *P* ≤ .05. All analyses were conducted with R version 3.5.2.

interaction between smoking rate and TST on 6MWT was significant (slope estimate, 0.02; *P* = .04); among heavier smokers (≥ 10 cpd),⁵¹ every additional minute of TST was associated with a 0.05 to 0.58 increase in 6MWT distance. For example, in a smoker from our sample who smoked 20 cpd, an additional 20 min of TST would be associated with an additional 4.40 m in the 6MWT (assuming all other model covariates were held constant; see [Table 3](#)). All model assumptions (linearity, homoscedasticity, normality of residuals, and no multicollinearity) were met.

Moderating Effects of SE on the Association Between Smoking Rate and 6MWT Distance

In a fully adjusted multivariable linear regression model of 6MWT that included an interaction term for smoking rate × SE as well as variables for the main effects of smoking rate, SE, and all study covariates, the smoking rate was significantly and negatively associated with 6MWT distance. For every additional cigarette smoked, the 6MWT distance covered was expected to decline by

12.44 m (slope estimate, -12.44 ; $P = .01$) (Table 4). The interaction between smoking rate and SE on 6MWT was significant (slope estimate, 0.18 ; $P = .01$): among smokers who smoked ≥ 10 cpd every additional percentage of SE was associated with a 0.84 to 6.17 increase in 6MWT distance covered. For example, in a smoker from our sample who smoked 20 cigarettes per day, an additional 10% sleep efficiency would be associated with an additional 26.2 m in the 6MWT (assuming all other model covariates were held constant; Table 5). All model assumptions (linearity, homoscedasticity, normality of residuals, and no multicollinearity) were met.

Discussion

AA adults bear disproportionate COPD-related morbidity and mortality. Sleep health metrics such as TST are emerging as critical prognostic factors in cardiometabolic health, but the role of sleep health in lung function is less well documented. The main and

novel finding from this study is that longer sleep duration and higher sleep efficiency may moderate the association between smoking rate and exercise tolerance in AA smokers. For example, our modeling suggested that among smokers who smoked 20 cpd, every additional minute of sleep time, and every additional percentage of SE, was associated with an additional 0.22 and 2.62 m, respectively, in the 6MWT. Given that the sample mean TST (5 h and 8 min) and SE (69%) were both well below the recommended 7 to 8 h TST⁵² and 90% SE,⁵² this could help explain a clinically meaningful decrease in functional capacity by 26 to 56 m in the 6MWT⁴⁴ seen in a one-pack-per-day smoker without apparent obstructive lung or cardiovascular disease. Thus, in conjunction with other smoking cessation efforts, sleep health may be an important therapeutic target to improve exercise capacity in AA smokers.

The reason why SE, and to a lesser extent, TST, was associated with significantly higher 6MWT distances in heavier vs lighter AA smokers is not clear. Plausible

Figure 1 – CONSORT diagram to show participant enrollment, assessment, and analysis. CONSORT = Consolidated Standards of Reporting Trials; GOLD = Global Initiative for Chronic Obstructive Lung Disease.

TABLE 1] Baseline Characteristics of Study Participants and Bivariate Association With 6-Min Walk Test Distance: N = 209

Study Variable	Summary Statistics ^a	Slope Estimate	P Value
Age, mean (SD), y	54.75 (5.96)	0.001	1.00
Sex, No. (%), male	86 (41.1%)	41.07	< .001
Education status, No. (%), < 8 y	161 (77.4%)	16.99	.19
BMI, mean (SD), kg/m ²	28.91 (5.99)	-2.43	.01
Smoking rate, mean (SD), cpd	8.71 (6.78)	-0.57	.49
Fagerström Test for Cigarette Dependence, mean (SD)	3.76 (2.07)	-1.00	.72
COPD Assessment Test, mean (SD)	13.89 (8.95)	-2.36	< .001
Modified Medical Research Council-Dyspnea, No. (%)	...	... ^b	< .001 ^c
0	94 (46.1%)	Ref	Ref
1	48 (23.5%)	-20.46	.12
2	26 (12.7%)	-37.02	.03
3	21 (10.3%)	-71.20	< .001
4	15 (7.4%)	-75.39	< .001
Carbon monoxide level, mean (SD), ppm	17.32 (12.16)	0.05	.92
6-Min walk test distance, mean (SD), m	346.62 (78.24)	...	...
Heart rate 1 min of recovery, mean (SD), bpm	88.16 (13.37)	0.54	.19
Oxygen saturation, mean (SD), %	98.16 (2.16)	7.73	.002
Sleep efficiency, mean (SD), %	69.90 (12.30)	0.39	.40
Total sleep duration, mean (SD), min	307.99 (92.20)	-0.02	.71
FEV ₁ , mean (SD), %	87.99 (22.34)	0.45	.07
FVC, mean (SD), %	100.23 (31.76)	0.34	.05
FEV ₁ /FVC ratio, mean (SD)	0.90 (0.14)	-32.47	.41
Apnea-hypopnea index, mean (SD)	5.62 (4.17)	-2.83	.03
Current medication use, No. (%)			
Antihypertensive medications	69 (33.0%)	-24.12	.04
Nodal blocker agents	13 (6.2%)	-22.91	.33
Antidepressants	41 (19.6%)	-25.59	.06
Statins	41 (19.6%)	-23.31	.09
Long-acting bronchodilators	23 (11.0%)	-0.63	.97
Diabetic medications	26 (12.4%)	5.26	.76

bpm = beats per minute; ppm = parts per million.

^aStatistics are either mean (SD) (continuous variables) or frequency (%) (discrete variables).

^bConventional slope estimates available only for individual levels.

^cP value obtained by one-way analysis of variance.

mechanisms for this association may be autonomic imbalance and inflammation. Heavier smokers have higher levels of autonomic imbalance, including higher resting heart rate and heart rate variability,⁵³ impaired 24-h cardiovascular sympathetic tone,⁵⁴ and blunted cerebrovascular autonomic regulation and baroreflex response to hypercapnia.⁵⁵ Sleep deprivation is also associated with autonomic imbalance.⁵⁶ Importantly, increased heart rate, and heart rate variability, predict increased cardiovascular risk and mortality.⁵⁷ Regarding inflammation markers, heavier smokers have higher

levels of C-reactive protein and IL-6.⁵⁸ This increased inflammation can lead to skeletal muscle weakness and a decrease in exercise capacity.⁵⁹ Sleep deprivation studies have shown similarly increased levels of inflammatory markers, which were associated with peripheral muscle weakness and decreased muscle strength.⁶⁰ Although the hypotheses that inflammation and autonomic imbalance may be mechanisms through which better sleep health promotes functional exercise capacity in ≥ 10 -cpd smokers cannot be tested in the current study, this warrants clinical investigation in future work.

TABLE 2] Multivariable Linear Regression Model to Test Independent Association, and Interaction, Between Smoking Rate and Sleep Duration on 6-Min Walk Test Distance Covered^a

Study Variable	Slope Estimate	95% CI	P Value
Smoking rate	-5.37	10.37 to -0.38	.04
Sleep duration	-0.14	-0.33 to 0.06	.18
FVC	0.32	-0.01 to 0.64	.05
Heart rate at 1 min of recovery	1.02	0.22 to 1.82	.01
Oxygen saturation	6.76	1.90 to 11.62	.01
Apnea-hypopnea index	-1.61	-3.79 to 1.48	.39
Smoking rate × sleep duration	0.02	0.00 to 0.03	.04

^aModel adjusted for age, biological sex, educational attainment (at least 8 y of schooling or not), BMI, Center for Epidemiologic Studies-Depression Scale, use of antihypertensives, use of nodal blockers, use of statins, use of COPD medication (long-acting muscarinic antagonist, long-acting β -agonist, or inhaled corticosteroid), use of diabetes medication, evidence of diabetes, oxygen saturation, FVC, apnea-hypopnea index, and 1-min resting heart rate.

Another finding from this study was that the magnitude of the association between the SE × smoking rate interaction was considerably greater than that of the TST × smoking rate interaction on 6MWT performance. SE is conceptualized as the percentage of time in bed that is spent asleep. As such, it encompasses several other sleep metrics including TST, sleep onset latency (ie, time it takes to fall asleep), night time awakenings, and to some extent, sleep timing. Protocols for cognitive behavioral therapy for insomnia (CBT-I) recommend that adult patients achieve a 95% SE rate

TABLE 4] Multivariable Linear Regression Model to Test Independent Association, and Interaction, Between Smoking Rate and Sleep Efficiency on 6-Min Walk Test Distance Covered^a

Study Variable	Slope Estimate	95% CI	P Value
Smoking rate	-12.44	-21.53 to -3.35	.01
Sleep efficiency	-0.94	-2.41 to 0.53	.21
FVC	0.30	-0.02 to 0.61	.07
Heart rate at 1 min of recovery	1.16	0.34 to 1.97	.01
Oxygen saturation	6.77	1.96 to 11.57	.01
Apnea-hypopnea index	-0.85	-3.47 to 1.76	.52
Smoking rate × sleep efficiency	0.18	0.05 to 0.31	.01

^aModel adjusted for age, biological sex, educational attainment (at least 8 y of schooling or not), BMI, Center for Epidemiologic Studies-Depression Scale, use of antihypertensives, use of nodal blockers, use of statins, use of COPD medication (long-acting muscarinic antagonist, long-acting β -agonist, or inhaled corticosteroid), use of diabetes medication, evidence of diabetes, oxygen saturation, FVC, apnea-hypopnea index, and 1-min resting heart rate.

before addressing the age-appropriate sleep duration recommendation.⁶¹ Poor sleep efficiency, outside of traditional OSA scoring, is predictive of myocardial infarction, stroke, and cardiovascular-related mortality risk.⁶² Moreover, deficits in sleep efficiency have been consistently demonstrated in smokers vs nonsmokers.^{32,63} Even nonsmokers who have been administered a transdermal patch report sleep deficits, including reduced sleep efficiency.^{64,65} Together, these data underscore the relationship between sleep efficiency and tobacco use.

TABLE 3] Improvement in 6-Min Walk Test Distance per Additional Minute of Sleep in Heavy Smokers^a

Cigarettes per Day	No. (%)	Change in Estimated 6MWT Distance (m)
10	31 (14.8%)	0.05
15	8 (3.8%)	0.13
20	22 (10.5%)	0.22
25	3 (1.4%)	0.31
30	1 (0.5%)	0.40
35	0 (0.0%)	0.49
40	1 (0.5%)	0.58

6MWT = 6-min walk test.

^aBased on model slope estimates and the assumption that all other covariates are held constant.

TABLE 5] Change in 6-Min Walk Distance per Additional Percentage of Sleep Efficiency in Heavy Smokers^a

Cigarettes per Day	No. (%)	Estimated 6MWT Change (m)
10	31 (14.8)	0.84
15	8 (3.8)	1.73
20	22 (10.5)	2.62
25	3 (1.4)	3.51
30	1 (0.5)	4.39
35	0 (0.0)	5.28
40	1 (0.5)	6.17

See Table 3 legend for expansion of abbreviation.

^aBased on model slope estimates and the assumption that all other covariates are held constant.

These data should be interpreted with consideration of the fact that these results cannot be extrapolated to other sociodemographic groups, because expected 6MWT performance can vary across populations and may not be fully explained by anthropomorphic differences.^{66,67} The generalizability of these results to adults with moderate-severe OSA is also not clear. The cross-sectional study design precludes an assessment of causality, and, results from this study do not provide insight into the mechanisms through which TST and SE may relate to lung function. In addition, the current study design did not fully account for participant factors that may have limited WatchPAT studies, including use of α -blockers or chronic atrial fibrillation. Nevertheless, these data extend current knowledge about the potential role of improved sleep

health in the functional exercise capacity of AA smokers. Future studies are needed to examine the extent to which changes in sleep health are associated with changes in lung and functional exercise capacity across time in smokers. The effects on inflammation and autonomic imbalance in this context have yet to be measured. Furthermore, the role of the circadian system or timing of activities such as sleep, activity, and smoking in exercise capacity is poorly understood. Data showing that systolic BP recovery following exercise is greatest in the afternoon⁶⁸ speak to the potential of this work. Future work in this area has the potential to clarify the interplay between smoking and its relationship with daytime activity and nocturnal sleep patterns before the development of overt lung disease.

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Author contributions: F. P. had full access to all of the data in the study and takes responsibility for the data analysis, data interpretation, and manuscript content. B. B. conducted the data analysis, and substantially contributed to the data interpretation and writing of this manuscript. A. S. and F. P. designed the study. A. S., A. J. G., M. Z., R. B., G. M., M. A. G., A. D., and G. J. C. contributed to data interpretation and the writing of the manuscript.

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Additional information: The e-Appendix can be found in the Supplemental Materials section of the online article.

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