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Original investigation

Effect of Tobacco Smoke Exposure on Functional Capacity, Respiratory Muscle Strength, and Physical Activity Level in Patients with Pulmonary Arterial Hypertension: A Preliminary Study

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ABSTRACT

Purpose: It is known that tobacco smoke exposure is a risk factor for the development of pulmonary arterial hypertension (PAH). In addition, tobacco smoke exposure can cause numerous health problems. This study aimed to compare functional capacity, respiratory muscle strength, and physical activity level between the patients with PAH who have or do not have tobacco smoke exposure.

Methods: Seventeen patients with PAH who has tobacco smoke exposure and 20 nonsmoker patients were included in this cross-sectional study. Tobacco smoke exposure was defined as current smokers, ex-smokers, and passive smokers. The study outcomes included the maximal inspiratory and expiratory pressure measurement, 6-minute walk test, and physical activity.

Results: There was no significant difference for age, gender, body mass index, pulmonary arterial pressure, and functional class between the two groups ($p>0.05$). Inspiratory muscle strength ($p=0.035$), functional exercise capacity ($p=0.040$) and physical activity level ($p=0.034$) were lower in patients with tobacco smoke expose compared to the nonsmokers.

Conclusion: The results of this study showed that functional capacity, respiratory muscle strength, and physical activity level were significantly lower in patients with tobacco smoke expose than the nonsmoker patients with PAH. These findings suggest that tobacco smoking is not only associated with PAH risk but also numerous health problems, specifically important ones for this population.

Keywords: pulmonary arterial hypertension, smoking, cigarette, exercise, rehabilitation

INTRODUCTION

Pulmonary arterial hypertension (PAH) is a condition that resting mean pulmonary artery pressure (mPAP) is equal or greater than 20 mmHg, pulmonary arterial wedge pressure (PAWP) it equal or less than 15 mmHg and pulmonary vascular resistance (PVR) is greater than 3 Wood units (WU) (1). PAH is considered as a subgroup of pulmonary hypertension (PH). In the pathophysiology of PAH, vasoconstriction is thought to lead to inflammation and endothelial dysfunction (2).

Environmental risk factors may play a role in the occurrence of PAH. One of the widespread environmental factors associated with systemic endothelial dysfunction is tobacco smoke (active and secondhand) (3). In addition, tobacco smoke affects the airways and lungs of people who are active smokers or passively exposed (4). In animal and human studies, exposure to tobacco smoke has been shown to lead to pulmonary endothelial dysfunction and PH (5, 6). Cigarette smoke-induced PH is associated with oxidative vascular damage caused by reactive nitrogen species, which are thought to be originated from cigarette smoke itself (7). In a study of young heavy smokers, pulmonary artery pressure was reported to be higher than nonsmokers (8). It has been shown that cigarette exposure is high in patients with PAH and that exposure to both active and environmental tobacco smoke is common in PH (3, 9, 10). Tobacco smoke exposure is also a risk factor for the development of PAH (3). It has been reported that 10–15%

of patients with PH continue to smoke after the diagnosis, and half of nonsmoker women with PH are exposed to secondhand smoking (10). In addition, it has been shown that smoking rate in patients with PAH is higher than both the patients with chronic thromboembolic PH and healthy controls (3, 10). In the studies of healthy people and patients with chronic obstructive pulmonary disease (COPD), the smokers were reported to have less physical activity level and exercise capacity than the nonsmokers (11–14). Exercise capacity has important impacts on prognosis, quality of life, and mortality in PAH (15). Increased respiratory and peripheral muscles strength and physical activity level are associated with increased exercise capacity in patients with PAH (15). Despite the known harm effects of tobacco smoke exposure, there is no study investigating the effects of cigarette exposure on functional exercise capacity, respiratory muscle strength, and physical activity level, which are the important endpoints in the assessment and rehabilitation of patients with PAH. Therefore, we aimed to compare functional exercise capacity, respiratory muscle strength, and physical activity level between patients with PAH who have and do not have tobacco smoke exposure.

METHODS

Study group

Thirty-seven patients with PAH were included in this cross-sectional study from the PH outpatient clinic of Dokuz Eylül University Hospital. The inclusion criteria were as follows: defined diagnosis of PAH, 18 years older above, and no change in the PAH-specific pharmaceutical therapy for the previous three months. The exclusion criteria were having an orthopedic problem which interferes with walking, left heart failure, and chronic obstructive pulmonary disease.

The Noninvasive Research Ethics Board of Dokuz Eylül University was approved the study protocol (approval number=2019/13–24). The study was performed following the ethical standards as laid down in the 1964 Declaration of Helsinki (as revised in Brazil 2013). All the participants gave the written informed consent before entering the study.

Outcome measurements

Demographic and clinical characteristics [New York Heart Association (NYHA) classification, brain natriuretic peptide, and pulmonary arterial pressure] of the patients were recorded.

Tobacco smoke exposure was defined as current smokers, ex-smokers, and passive smokers. If a person smoked ≥1 packet of cigarettes for over 1 year ever was accepted as current or ex-smoker. If a person has not been ever smoked but reported exposure to secondhand smoke ≥1 hour in a day for ≥1 year was accepted as passive smoker. The pack-years of smoking was calculated as "number of packs of cigarettes smoked per day × number of years the person had been smoked."

Respiratory muscle strength

The respiratory muscle strength was assessed as maximal inspiratory pressure (MIP) and maximal expiratory pressure (MEP) with a hand-held mouth pressure device (Micro RMP; Micro Medical, Rochester, UK). Three to five acceptable and reproducible maximal maneuvers were performed in the assessment of MIP and MEP (16).

Functional exercise capacity

The functional exercise capacity was measured by the six-minute walk test (6MWT) following the standard guidelines in a 30-m indoor corridor (17). The distance walked in the 6MWT (6MWD) was recorded as the score.

Physical activity

The physical activity level was assessed using the Turkish version of the International Physical Activity Questionnaire-Short Form (IPAQ-SF) which is a 7-item questionnaire asking the frequency and duration of some activities done in the last 7 days (18, 19). The metabolic equivalents (MET)-minutes/week was calculated for each category by multiplying standard coefficient x minutes x days reported by the patients. The standard coefficients are 3.3 for walking category, 4.0 for moderate-intensity activity category, and 8.0 for vigorous-intensity activity category. The combined total physical activity MET-minutes/week was computed as the sum of walking + moderate + vigorous MET-minutes/week scores.

Statistical Analysis

Statistical significance was defined at p>0.05. The statistical analysis was conducted using the IBM SPSS software (Version 24.0, IBM Corp., Armonk, NY). Nonparametric analyses were used because the data were not normally distributed, as determined by Shapiro-Wilk test and histograms. The Mann-Whitney U test was used to compare the two groups in the continuous variables, and chi-square test was used to compare the categorical variables. The effect size was calculated as Cohen's d which was interpreted as small (d=0.2), moderate (d=0.5), and large (d=0.8) (20). Since the number of male patients were relatively small, the results for only female patients were also reported separately.

RESULTS

Seventeen patients (13 females) with tobacco smoke exposure and 20 nonsmoker patients (16 females) were included in the study. Comparisons of the characteristics of the patients are presented in Table 1. There was no significant difference for age, gender, body mass index, pulmonary arterial pressure, and functional class between the two groups (p>0.05). Median pulmonary arterial pressure was 59.50 (IQR, 46.00–98.75) mmHg, and brain natriuretic peptide level was 111.50 (IQR, 53.25–242.75) pg/ml for the patients with PAH who has tobacco smoke exposure. Median pulmonary arterial pressure was 56.00 (IQR, 46.00–76.25) mmHg, and brain natriuretic peptide level was 143.00 (IQR, 61.50–323.00) pg/ml for the patients who are nonsmokers. There were 8 patients (47.10%) with NYHA functional class II and 9 patients (52.90%) with class III in the tobacco smoke exposure group, and there were 14 patients (70.00%) with NYHA functional class II and 6 patients (30.00%) with class III in the nonsmoker group.

Table 1. Differential characteristics of smokers-passive smokers and nonsmokers who have PAH

	Smokers (n=17)		Nonsmokers (n=20)			
Variables	**Median (IQR)**	**Min-Max**	**Median (IQR)**	**Min-Max**	**p**	**d**
Age (years)	59.0 (45.50–64.00)	35.0–75.0	56.50 (34.75–67.50)	20.0–74.0	0.522	0.21
Gender, n (%)						
Female	13 (76.50)		16 (80.0)		0.795	0.09
Male	4 (23.50)		4 (20.0)			
Body mass index (kg/m^2)	28.39 (23.17–30.77)	19.72–34.96	25.97 (22.42–28.16)	18.82–39.04	0.263	0.39
NYHA classification, n (%)						
Class II	8 (47.1)		14 (70.00)		0.157	0.48
Class III	9 (52.9)		6 (30.00)			
mPAP (mmHg)	59.50 (46.00–98.75)	33.00–110.00	56.00 (46.00–76.25)	25.00–125.00	0.717	0.13
BNP level (pg/ml)	111.50 (53.25–242.75)	8.00–405.00	143.00 (61.50–323.00)	32.00–616.00	0.408	0.29
Tobacco smoke exposure (pack-years)	12.5 (6.00–20.00)	2.00–40.00	NA	NA	NA	NA

NYHA: New York Heart Association; **mPAP:** mean pulmonary arterial pressure; **BNP:** brain natriuretic peptide; **PAH:** pulmonary arterial hypertension.

Table 2. Comparison of muscle strength, functional capacity, physical activity between smokers-passive smokers and nonsmokers who have PAH

	Smokers (n=17)		Nonsmokers (n=20)			
Variables	**Median (IQR)**	**Min-Max**	**Median (IQR)**	**Min-Max**	**p**	**d**
MIP (cmH_2O)	44.00 (25.00–59.00)	12.00–87.00	56.50 (45.00–76.20)	30.00–101.00	0.035*	0.74
MEP (cmH_2O)	75.00 (50.00–107.00)	15.00–180.00	74.50 (57.00–106.50)	45.00–138.00	0.714	0.12
6MWD (m)	300.00 (210.00–435.00)	50.00–600.00	420.00 (337.50–480.00)	260.00–540.00	0.040*	0.71
IPAQ (MET-min/week)	99.00 (16.50–328.50)	0.00–891.00	297.50 (152.87–406.37)	33.00–842.00	0.034*	0.74

MIP: maximal inspiratory pressure; **MEP:** maximal expiratory pressure; **6MWD:** six-minute walk test distance; **IPAQ:** international physical activity questionnaire

Table 3. Comparison of muscle strength, functional capacity, physical activity in female smokers-passive smokers and nonsmokers who have PAH

	Smokers (n=13)		Nonsmokers (n=16)			
Variables	**Median (IQR)**	**Min-Max**	**Median (IQR)**	**Min-Max**	**p**	**d**
MIP (cmH_2O)	40.00 (24.00–46.50)	12.00–64.00	51.50 (45.00–65.00)	30.00–82.00	0.009*	1.10
MEP (cmH_2O)	64.00 (20.00–85.00)	15.00–107.00	71.50 (52.00–100.00)	45.00–118.00	0.300	0.40
6MWD (m)	270.00 (130.00–380.00)	50.00–420.00	420.00 (337.50–472.50)	260.00–520.00	0.001*	1.51
IPAQ (MET-min/week)	60.00 (0.00–183.50)	0.00–822.00	297.00 (115.75–391.50)	33.00–696.50	0.004*	1.23

MIP: maximal inspiratory pressure; **MEP:** maximal expiratory pressure; **6MWD:** six-minute walk test distance; **IPAQ:** international physical activity questionnaire

Active and passive tobacco smoke exposure was 12.5 pack-years. Six (35.5%) of the patients were current smokers, and they continued to smoke even after diagnosis, 8 (47.1%) of the patients were ex-smokers, and 3 (17.6%) of the patients were passive smokers. Of the 6 patients who continued smoking, 5 (83.3%) were female. All passive smokers were female. Two (66%) of the patients reported that their exposure to tobacco smoke had ended. Three (37.5%) of 8 patients who were ex-smokers were male, and 5 patients (62.5%) were female.

The comparison statistics results of respiratory muscle strength, functional exercise capacity, and physical activity level for the patients are presented in Table 2. The MIP was significantly lower in the patients who has tobacco smoke expose compared to the nonsmokers (p=0.035). The 6MWD was significantly shorter in tobacco smoke exposure group compared to the nonsmokers (p=0.040). Tobacco smoke exposure group's physical activity level was significantly lower than the nonsmoker group (p=0.034). The comparison of respiratory muscle strength, functional exercise capacity, and physical activity level for the only female patients with PAH are presented in Table 3. Tobacco smoke exposure group's MIP, 6MWD and physical activity level were significantly lower than the nonsmoker group (respectively; p=0.009, p=0.001, p=0.004) in female patients with PAH.

DISCUSSION

The aim of this study was to compare functional exercise capacity, respiratory muscle strength, and physical activity level between patients with PAH who have and do not have tobacco smoke exposure. The results showed that functional exercise capacity, inspiratory muscle strength, and physical activity level were significantly lower in the patients with PAH who has tobacco smoke expose than the patients who are nonsmokers. Functional exercise capacity, inspiratory muscle strength, and physical activity level were significantly lower in the female patients with PAH who has tobacco smoke expose than the female patients with PAH who are non-smokers. To our knowledge, this is the first study on comparing respiratory muscle strength and physical activity level between the patients with PAH who has and do not have tobacco smoke exposure.

In our study, 76.5% of the patients who has tobacco smoke expose were female. On the other hand, previous studies reported less numbers. For example, Keusch et al. (10) and Schiess et al. (3) reported the frequency of female patients who had ever exposed to tobacco smoke were 37% and 45%, respectively. Specifically, secondhand smoking was higher in women. These results suggest that women are significantly at more danger in terms of smoking exposure. Therefore, it is important to include the other family members, commonly the partners, of the women into the smoking cessation programs.

We found that the patients who have tobacco smoke exposure had significantly lower functional exercise capacity and physical activity level than the patients who do not have tobacco smoke exposure. In addition, female patients who have tobacco smoke exposure showed lower significantly lower functional exercise capacity, inspiratory muscle strength and physical activity level compared to nonsmoker women in our study. Physical inactivity is more common in smokers (21). A study showed that exercise capacity was lower in women compared to man in passive smokers in patients with PH (10). The previous studies showed that lower physical activity level and reduced exercise capacity was found in the smokers without COPD compared to nonsmokers (11, 22, 23). In addition, reduced exercise capacity has shown in smoker older people compared with nonsmoker older people (24). The muscle-lung-heart axis may cause reduced exercise capacity in smokers (25, 26). Physical activity and smoking are inversely related as physical activity and exercise can decrease inflammatory markers associated with decreased cardiovascular fitness (27). Our study can support that this mechanism could be similar in the patients with PAH. Since one of the main aims of the PAH management is to increase the exercise capacity, the issue of changing smoking behavior should be more important as a risk factor that can be changed.

We found that inspiratory muscle strength was significantly lower in the patients with PAH who has tobacco smoke exposure. The previous studies showed that healthy smoker individuals had reduced inspiratory muscle strength compared to the nonsmokers (28, 29). Enright et al. (30) showed significantly lower maximal inspiratory pressure in the older people who are current smokers than those who are the nonsmokers. Since the respiratory muscle strength is an important endpoint in the assessment and rehabilitation of the patients with PAH, our study suggests that smoking history, even secondhand, is very important. Future longitudinal studies are highly required to assess the effects of smoke quitting programs of these variables in the patients with PAH.

There are some potential limitations to our study. First, because of the cross-sectional design, we cannot provide a cause-effect relationship, longitudinal studies are highly warranted. Second, there is no healthy control group. A healthy control group would be better to understand how much the assessed variables were affected. Nicotine addiction level was not evaluated; but, it should be evaluated in further studies. Last, our sample size was quite low since it was a preliminary study. Our post-hoc sample size calculation revealed that 54 patients with PAH (27 in each group) should be required to achieve 80% of power with alpha error probability of 0.05 for the 6MWD as the primary outcome. We believe that our study will guide the future studies.

In conclusion, the patients with PAH who have active, or secondhand tobacco smoke exposure had significantly less functional exercise capacity, inspiratory muscle strength, and physical activity level compared to the nonsmokers. Also, the results were similar in the female patients who have active, or secondhand tobacco smoke exposure had significantly less functional exercise capacity, inspiratory muscle strength, and physical activity level compared to the nonsmokers. These findings can be important for patients with PAH and their caregivers, as early counselling to smoking cessation for both the patients themselves and their close relatives can be important to maintain and/or improve functional exercise capacity, inspiratory muscle strength, and physical activity level. However, longitudinal prospective studies with larger sample size are highly warranted to prove this hypothesis.

Informed Consent: All the participants gave the written informed consent before entering the study.

Compliance with Ethical Standards: Noninvasive Research Ethics Board of Dokuz Eylül University (22.05.2019)

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REFERENCES

1. Simonneau G, Montani D, Celermajer DS, et al. Haemodynamic definitions and updated clinical classification of pulmonary hypertension. Eur Respir J 2019;53:1801913. [CrossRef]
2. Rabinovitch M. Molecular pathogenesis of pulmonary arterial hypertension. J Clin Invest 2012;122:4306-4313. [CrossRef]
3. Schiess R, Senn O, Fischler M, et al. Tobacco smoke: a risk factor for pulmonary arterial hypertension? A case-control study. Chest 2010;138:1086-1092. [CrossRef]
4. Gibbs K, Collaco JM, McGrath-Morrow SA. Impact of Tobacco Smoke and Nicotine Exposure on Lung Development. Chest 2016;149:552-561. [CrossRef]
5. Wright JL, Tai H, Churg A. Cigarette smoke induces persisting increases of vasoactive mediators in pulmonary arteries. Am J Respir Cell Mol Biol 2004;31:501-509. [CrossRef]
6. Barberà JA, Peinado VI, Santos S, Ramirez J, Roca J, Rodriguez-Roisin R. Reduced expression of endothelial nitric oxide synthase in pulmonary arteries of smokers. Am J Respir Crit Care Med 2001;164:709-713. [CrossRef]
7. Wright JL, Zhou S, Churg A. Pulmonary hypertension and vascular oxidative damage in cigarette smoke exposed eNOS(-/-) mice and human smokers. Inhal Toxicol 2012;24:732-740. [CrossRef]
8. Naser H, Hadi N, Ibrahim A, Assad A. Study the Pulmonary Hypertension among Heavy Smokers Young Adult Males before the Clinical Evidences of Chronic Lung Disease. J Clin Exp Cardiolog 2017;8:2. [CrossRef]
9. Ling Y, Johnson MK, Kiely DG, et al. Changing demographics, epidemiology, and survival of incident pulmonary arterial hypertension: results from the pulmonary hypertension registry of the United Kingdom and Ireland. Am J Respir Crit Care Med 2012;186:790-796. [CrossRef]
10. Keusch S, Hildenbrand FF, Bollmann T, et al. Tobacco smoke exposure in pulmonary arterial and thromboembolic pulmonary hypertension. Respiration 2014;88:38-45. [CrossRef]
11. Furlanetto KC, Mantoani LC, Bisca G, et al. Reduction of physical activity in daily life and its determinants in smokers without airflow obstruction. Respirology 2014;19:369-375. [CrossRef]
12. Moslemi-Haghighi F, Rezaei I, Ghaffarinejad F, Lari R, Pouya F. Comparison of Physical Fitness among Smoker and Non-Smoker Men. Addict Health 2011;3:15-19. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3905518/
13. Ibrahim AA. Impact of smoking on aerobic capacity in young adult smokers. Int J Med Res Health Sci 2016;5:26-30. https://www.ijmrhs.com/medical-research/impact-of-smoking-on-aerobic-capacity-in-young-adult-smokers.pdf
14. Caram LMO, Ferrari R, Bertani AL, et al. Smoking and Early COPD as Independent Predictors of Body Composition, Exercise Capacity, and Health Status. PLoS One 2016;11:e0164290. [CrossRef]
15. Tran DL, Lau EM, Celermajer DS, Davis GM, Cordina R. Pathophysiology of exercise intolerance in pulmonary arterial hypertension. Respirology 2018;23:148-159. [CrossRef]
16. Black LF, Hyatt RE. Maximal respiratory pressures: normal values and relationship to age and sex. Am Rev Respir Dis 1969;99:696-702. https://pubmed.ncbi.nlm.nih.gov/5772056/
17. American Thoracic Society (ATS) statement: guidelines for the six-minute walk test. Am J Respir Crit Care Med 2002;166:111-117. [CrossRef]
18. Saglam M, Arikan H, Savci S, et al. International physical activity questionnaire: reliability and validity of the Turkish version. Percept Mot Skills 2010;111:278-284. [CrossRef]
19. Craig CL, Marshall AL, Sjostrom M, et al. International physical activity questionnaire:12-country reliability and validity. Med Sci Sports Exerc 2003;35:1381-1395. [CrossRef]
20. Cohen J. Statistical power analysis for the behavioral sciences, 2nd ed. NJ, USA: Erbaum Press, Hillsdale; 1988. http://www.utstat.toronto.edu/~brunner/oldclass/378f16/readings/CohenPower.pdf
21. Lee IM, Shiroma EJ, Lobelo F, Puska P, Blair SN, Katzmarzyk PT; Lancet Physical Activity Series Working Group. Effect of physical inactivity on major non-communicable diseases worldwide: an analysis of burden of disease and life expectancy. Lancet 2012;380:219-229. [CrossRef]
22. Elbehairy AF, Guenette JA, Faisal A, et al. Mechanisms of exertional dyspnoea in symptomatic smokers without COPD. Eur Respir J 2016;48:694-705. [CrossRef]
23. Woodruff PG, Barr RG, Bleecker E, et al. Clinical Significance of Symptoms in Smokers with Preserved Pulmonary Function. N Engl J Med 2016;374:1811-1821. [CrossRef]
24. Mesquita R, Gonçalves CG, Hayashi D, et al. Smoking status and its relationship with exercise capacity, physical activity in daily life and quality of life in physically independent, elderly individuals. Physiotherapy 2015;101:55-61. [CrossRef]
25. Muller PT, Barbosa GW, O'Donnell DE, Neder JA. Cardiopulmonary and Muscular Interactions: Potential Implications for Exercise (In) tolerance in Symptomatic Smokers Without Chronic Obstructive Pulmonary Disease. Front Physiol 2019;10:859. [CrossRef]
26. Barn P, Giles L, Héroux ME, Kosatsky T. A review of the experimental evidence on the toxicokinetics of carbon monoxide: the potential role of pathophysiology among susceptible groups. Environ Health 2018;17:13. [CrossRef]
27. Garcia-Aymerich J, Lange P, Benet M, Schnohr P, Antó JM. Regular physical activity modifies smoking-related lung function decline and reduces risk of chronic obstructive pulmonary disease: a population-based cohort study. Am J Respir Crit Care Med 2007;175:458-463. [CrossRef]
28. Bostanci Ö, Mayda H, Yılmaz C, Kabadayı M, Yılmaz AK, Özdal M. Inspiratory muscle training improves pulmonary functions and respiratory muscle strength in healthy male smokers. Respir Physiol Neurobiol 2019;264:28-32. [CrossRef]
29. Formiga MF, Campos MA, Cahalin LP. Inspiratory Muscle Performance of Former Smokers and Nonsmokers Using the Test of Incremental Respiratory Endurance. Respir Care 2018;63:86-91. [CrossRef]
30. Enright PL, Kronmal RA, Manolio TA, Schenker MB, Hyatt RE. Respiratory muscle strength in the elderly. Correlates and reference values. Cardiovascular Health Study Research Group. Am J Respir Crit Care Med 1994;149:430-438. [CrossRef]