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EFFECTS OF SMOKING ON RESPIRATORY FLOWS IN YOUNG, PHYSICALLY ACTIVE ADULTS

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Abstract. The prevalence of respiratory diseases in Lithuania, such as chronic bronchitis, chronic obstructive pulmonary disease (COPD), emphysema, and asthma, has been increasing across all age groups. Similarly, smoking rates among young people in Lithuania are high, with one in five young adults reporting that they smoke. While there are extensive long-term studies on the health effects of tobacco and its strong link to various pathologies, there is still limited knowledge about the short-term health effects of smoking, especially e-cigarettes, among young adults. The aim of our study was to evaluate and compare pulmonary parameters in non-smoking and smoking physically active and non-active adults. Spirometry, a widely used method for respiratory functional diagnostics, was used to test self-reported physically active and non-physically active smokers and non-smokers. The main results show that physically active non-smokers had significantly higher respiratory flows compared to other groups. Additionally, e-cigarette smokers have significantly lower inspiratory flows compared to all other groups. While all groups exhibit normal lung resistance, tobacco smokers have significantly higher resistance compared to e-cigarette smokers. Physically active males who smoke e-cigarettes have a smaller PIF/PEF ratio, indicating enhanced additional clearance due to mechanically stimulated airway flow. In conclusion, these studies provide valuable insights into pulmonary ventilatory function and have implications for understanding the impact of new tobacco alternatives on young people. Physical activity partially blunts the changes in the respiratory system caused by at least two years of smoking e-cigarettes or tobacco cigarettes.
Keywords: spirometry, flows, smoking, physical activity

Introduction

Smoking is a societal problem, and the chronic obstructive pulmonary disease (COPD) it causes is currently the third most common cause of morbidity and mortality worldwide (Agarwal et al., 2021). The prevalence of respiratory diseases in Lithuania, such as chronic bronchitis, COPD, emphysema, and asthma, has shown an increasing trend across all age groups (Health of Population of Lithuania, 2020). Furthermore, smoking remains one of the most common risk factors for developing respiratory diseases. Among young people in Lithuania, the prevalence of smoking is high, with one in five young adults reporting that they smoke (Health of Population of Lithuania, 2020) and e-cigarette[1] use among young people in Lithuania has surpassed tobacco cigarette smoking since 2019, according to ESPAD survey data (European Monitoring Centre for Drugs and Drug Addiction, 2020).

It is known that, compared to smoking, the use of vaping products leads to a substantial reduction in biomarkers of toxicant exposure associated with cigarette smoking (McNeill et al., 2022). In addition, the thermal degradation by-products formed during vapor generation (Sleiman et al., 2016) can result in degradation products such as metals, carbonyls, and other organic compounds that contribute to pulmonary pathogenesis (Rebuli et al., 2023). Interestingly, in some European countries, the majority of the population perceives e-cigarettes to be equally or more harmful than combustible cigarettes. However, the same research reports that one-third of respondents believe e-cigarettes are less harmful than combustible cigarettes (Gravely et al., 2020). Furthermore, the use of e-cigarettes or vaping products can cause e-cigarette or vaping product use–associated lung injury (EVALI), a severe pulmonary illness (Rebuli et al., 2023). However, there is still limited knowledge about the long-term health effects of e-cigarette ingredients. While there is an increasing body of evidence regarding e-cigarettes' effects on the respiratory system, these findings often contradict each other (Qureshi et al., 2023), indicating that more research is needed. The prevalence of respiratory diseases is higher among smokers than non-smokers. Those who smoked cigarettes during the 25-year follow-up period were found to be more likely than non-smokers to have chronic obstructive pulmonary disease: 36% of smokers compared to 8% of non-smokers, respectively (Zheng et al., 2000). Evidence suggests that a deficiency in antioxidant vitamins (vit. C and vit. E) may be an additional risk factor for smokers, as the body is unable to defend itself against the destructive effects of oxidative radicals from cigarette smoke (Weiss, 2021).

[1] E-cigarettes in this study was an e-cigarette, vape pen or other electronic nicotine delivery system which heated a liquid of nicotine, flavouring, propylene glycol and other additives into an aerosol that was inhaled through a mouthpiece.

Body plethysmography and diffusing capacity measurement with routine spirometry can provide valuable information for detection of changes reflecting to the early onset of pulmonary pathologies (Nagelmann et al., 2011). Even more, it is reported that forced flow parameters like $FEF_{25-75\%}$ values in patients with normal lung function can predict the development of chronic obstructive pulmonary disease (COPD) (Kwon et al., 2020). However, there is still limited knowledge about the short-term smoking effects on young physically active healthy adults.

The aim of our study was to evaluate and compare pulmonary parameters in non-smoking and smoking physically active and non-active adults.

Methods

Study design and sample. A total of 83 male second-year medical students of Lithuanian University of Health Sciences, Medical academy, Medical faculty (mean age 21.05±0.03 years) participated in the study.

The subjects were divided into 4 groups: a control (C) group of non-physically active and non-smoking males (20 subjects), a group of physically active (PA) males (20 subjects), a group of physically active and e-cigarette-smoking males (PA+e-cig) (20 subjects), and physically active and tobacco cigarette-smoking males (PA+t-cig) (23 subjects).

The physically active groups consisted of subjects who reported exercising vigorously for at least 1 hour daily or several times a week in their leisure time during the last 2 years, however students who exercised a few times a month or less were classified as non-physically active. Subjects who smoke tobacco cigarettes smoke on average 10-13 tobacco cigarettes per day, with a smoking duration of at least 2-3 years.

Definition of E-cigarettes in this study was an e-cigarette, vape pen or other electronic nicotine delivery system which heated a liquid of nicotine, flavouring, propylene glycol and other additives into an aerosol that was inhaled through a mouthpiece. E-cigarettes were consumed in 4-7 days with a smoking duration of at least 2-3 years.

Forced spirometry and protocol. Forced spirometry (Spirometer EK56, Hellige, Freiburg, Germany) was performed in accordance with methodical requirements., the expiratory period lasted 6 seconds and according to protocol, the recording started with a rapid onset of forced expiration and ended with forced inspiration.

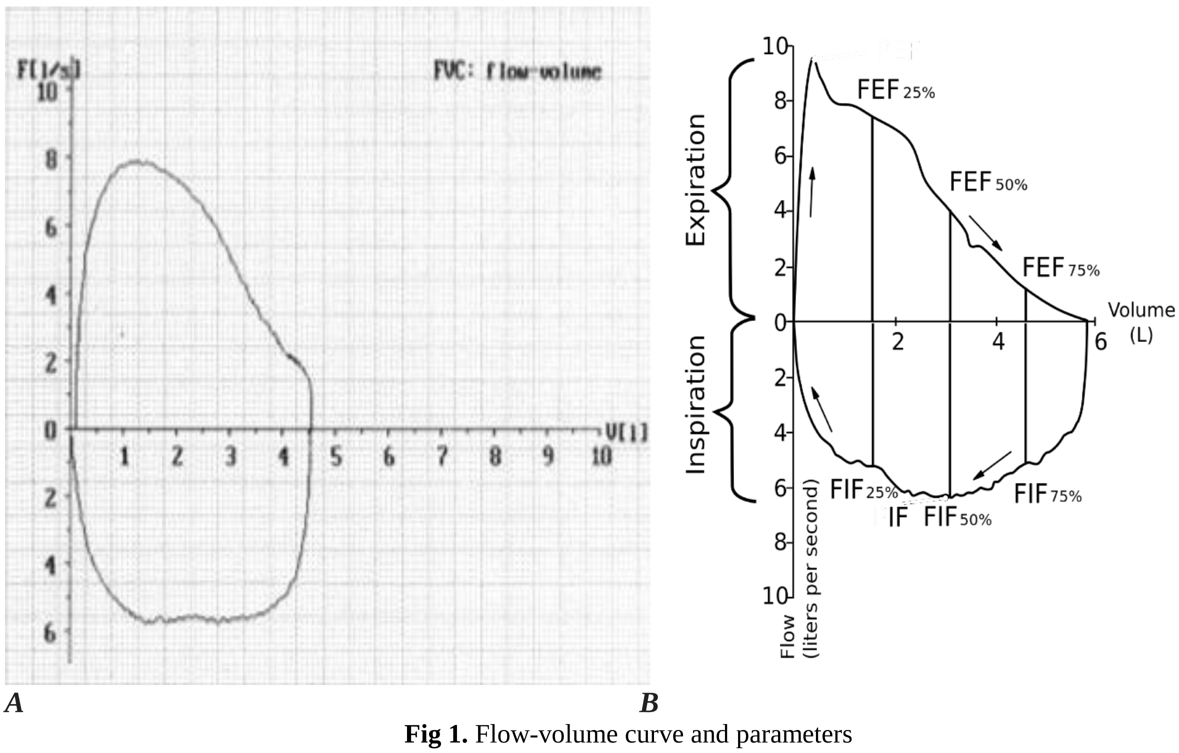

Fig 1. Flow-volume curve and parameters
A Flow-volume curve recording; B Flow parameters of Flow-volume curve

At least 3 spirograms were suitable for evaluation from each participant and all used spirogram recordings were free of artefacts (see Fig.1 A for an example of recorded spirogram).

Before the spirometry, the subjects were not smoking and eating or drinking for at least 2h prior to the test. Throughout all recording the subjects were in a sitting position, with the nose clamped to prevent air leakage through the nose and after inspiration as deeply as possible (unforced) expiration was as forcefully blew in the mouthpiece as sharply as possible (forced) without holding followed deep inspiration through a mouthpiece (forced) until the end.

Spirometric parameters. Spirometry, a widely used method for respiratory functional diagnostics, was used in this study to analyse and compare respiratory function parameters among different study groups (Fig.1 B). The following spirometric parameters (Miller et al., 2005) were assessed during the study:

Expiratory parameters: Peak expiratory flow (PEF, l/s), forced expiratory flows at 75%, 50% and 25% of FVC ($FEF_{75\%}$, $FEF_{50\%}$ and $FEF_{25\%}$, respectively in L/s),

Inspiratory parameters: Peak inspiratory flow (PIF, l/s) and Forced inspiratory flow at 25% 50% and 75% of IVC ($FIF_{25\%}$, $FIF_{50\%}$ and $FIF_{75\%}$, respectively in L/s).

Respiratory ratios: The FEV1/FVC ratio, also known as the modified Tiffeneau-Pinelli index, represents the proportion of a person's vital capacity that they can expire in the first second of forced expiration (FEV_1) relative to the forced vital capacity (FVC). The $PIF/FEF_{50\%}$ ratio represents the proportion of forced peak inspiratory flows to forced expiratory flows at 50% of FVC.

The calculation of predicted norms took in consideration the gender, age, hight and body mass and was done my equipment (Spirometer EK56, Hellige, Freiburg, Germany) inbuild software algorithms. Ratio of peak inspiratory flow and peak expiratory flow (PIF/PEF ratio) and the expiratory time constant (RC_{EXP}). RC_{EXP} is the parameter that refers to the length of time required for a lung unit to fill or empty (Ikeda et al., 2018) and RC_{EXP} is defined as the product of airway resistance and lung compliance (Mead, 1978) and the variable serves as a dynamic measurement that can reflect the mechanical properties of the respiratory system (Ikeda et al., 2018). In our study, the value of RC_{EXP} was calculated according to Ikeda and co-workers (Ikeda et al., 2018) by using the equation:

$$RC_{EXP} = \frac{0.25 * FVC}{FEF50\text{-}FEF25}$$

Statistical analysis. The results of numerical values were expressed as mean ± standard deviation. For comparisons of different group measurements, an unpaired Student's t-test was used for parametrically distributed data, and the Mann-Whitney U test was used for non-parametrically distributed data. The Kolmogorov-Smirnov test was used to evaluate data distribution. Statistical significance was set at a P-value < 0.05. All analyses were carried out using the SPSS statistical program, version 22.0 (IBM SPSS, Inc., Chicago, IL, USA).

Results

The performance measures in this study of all respondents in all groups had normal respiratory parameters (Table 1) indicating that there are no clinically significant changes of the respiratory system, and no restrictive, obstructive or mixed pathologies. Nevertheless there exist statistically significant differences between groups, for example, physically active (PA) non-smokers had larger FVC and FEV_1 (Table 1). Similarly, forced expiratory flows where larger in PA group comparing to non-physically active control (C) or smoking groups (PA + e-cig or PA + t-cig). Additionally, e-cigarette smokers had significantly lower forced inspiratory flows and $PIF/FEF_{50\%}$ ratio compared to all other groups (Table 1).

Table 1 Comparative spirometric performance

PARAMETERS	C	PA	PA+ e-cig	PA+ t-cig.
Sample size (n)	20	20	20	23
Volumes				
FVC, L	4.68 ± 0.59	5.36 ± 0.71 *	4.55 ± 0.76	4.85 ± 0.63
FVC, %	84 (79-93) £	93 (87-108)	77 (75-93) £	89 (83-95)
FEV1, L	4.37(4.13-4.92)	5.03(4.85-5.44) *	4.38(3.96-4.41)	4.52(4.11-4.85)
Ratios				
FEV1/FVC ratio	0.95 (0.93-1.00)	0.96 (0.93-1.00)	0.99 (0.90-1.00)	0.98 (0.90-1.00)
PIF/$FEF_{50\%}$ ratio	1.10 (0.86-1.25)	0.91 (0.86-1.10)	0.78 (0.62-0.88) *	0.99 (0.90-1.15)
Flows of forced inspiration				
PIF, L/s	6.65 (5.61-8.56)	7.14 (6.47-7.76)	5.25 (5.15-5.80) *	6.47 (5.76-7.96)
$FIF_{25\%}$, L/s	5.70 (4.92-7.36)	6.56 (5.53-7.16)	4.55 (4.13-4.77) *	5.97 (5.33-7.32)
$FIF_{50\%}$, L/s	6.27 (4.85-8.40)	6.90 (6.28-7.76)	5.01 (4.94-5.30) *	6.43 (5.31-7.33)
$FIF_{75\%}$, L/s	6.06 (4.55-7.58)	6.29 (5.90-6.58)	5.16 (4.86-5.50) *	5.87 (5.00-6.40)
Flows of forced expiration				
PEF, L/s	8.67 ±1.26	9.16 ±1.27	8.68 ±0.79	8.00 ±1.67 £
PEF, %	83 (76-97)	89 (85-95)	81 (79-91)	77 (67-92)
$FEF_{25\%}$, L/s	3.69 (3.27-4.44)	3.99 (3.75-5.55)	5.75 (3.10-5.89)	4.53 (3.57-5.39)
$FEF_{25\%}$, %	132 (124-169)	147 (129-193)	174 (121-207)	166 (131-201)
$FEF_{50\%}$, L/s	6.32 (5.89-6.92) £	7.43 (6.80-8.00)	8.21 (6.24-8.63)	6.59 (5.65-6.96) £
$FEF_{50\%}$, %	112 (100-125) £	125 (119-133)	128 (107-146)	111 (99-123) £
$FEF_{75\%}$, L/s	8.97 (7.41-9.35)	8.94 (8.12-9.47)	8.00 (7.41-8.30) £	7.66 (6.71-8.68) £
$FEF_{75\%}$, %	100 (88-108)	101 (95-107)	89 (89-93) £	89 (78-99) £
$FEF_{25\%-75\%}$, L/s	5.80 (5.46-6.39) £	6.61(6.07-7.52)	5.88(5.66-7.87)	6.11(4.82-6.69)

Data shown as mean ± S.D. when normally distributed. Otherwise, data shown as median (25 percentile value-75percentile value). £-difference between PA; *-different from all other groups. Significances level P<0,05

There was a statistically significant difference between smoking groups (PA+e-cig = 0.45 (0.40-0.53) vs PA+t-cig= 0.56 (0.42-0.69); P<0.05) regarding the measurement of the expiratory time constate (RC_{EXP}). In addition, the PIF/PEF ratio (Figure 3) indicated a statistically significant difference between physically active e-cigarettes smoking group (PA+e-cig) and all other groups.

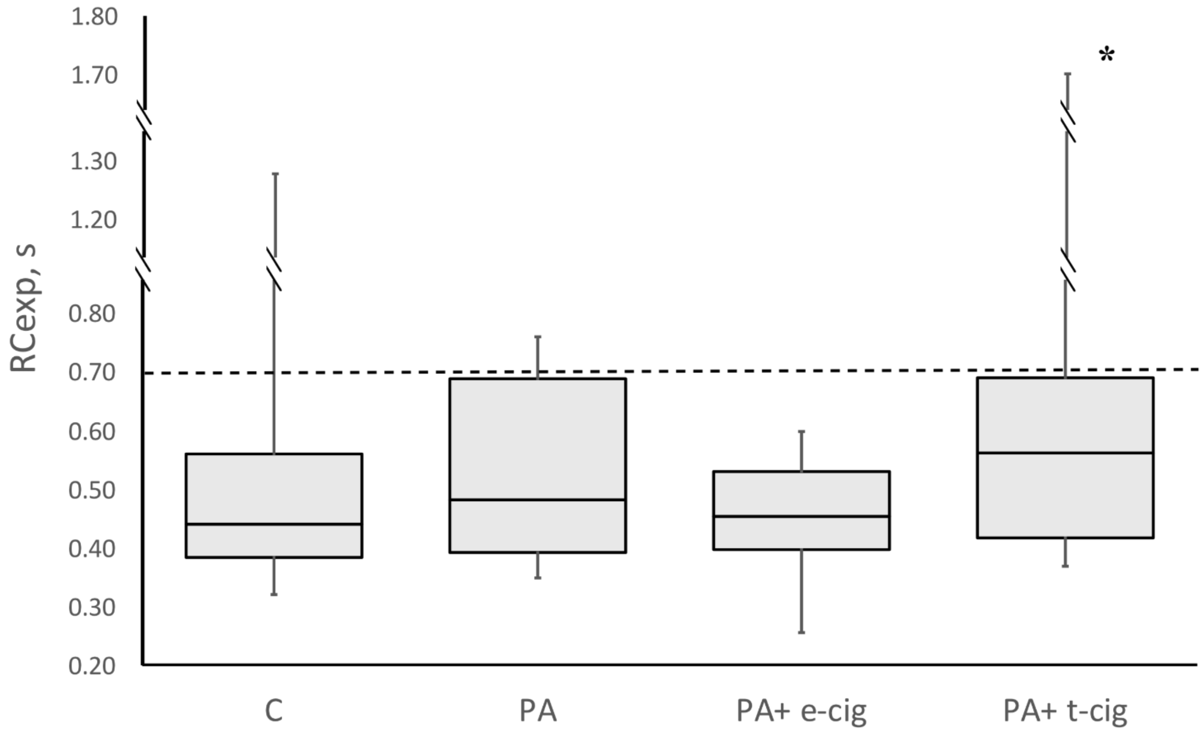

Fig. 2 The expiratory time constant (RC_{EXP})
Dashed line - $RC_{EXP} > 0.7$ seconds indicates an increase in lung resistance (Eghtedari et al., 2021), *- statistically significant difference between PA+ e-cig and PA+ t-cig groups

In addition, the PIF/PEF ratio (Figure 3) indicated a statistically significant difference between physically active e-cigarettes smoking group (PA+e-cig) and all other groups.

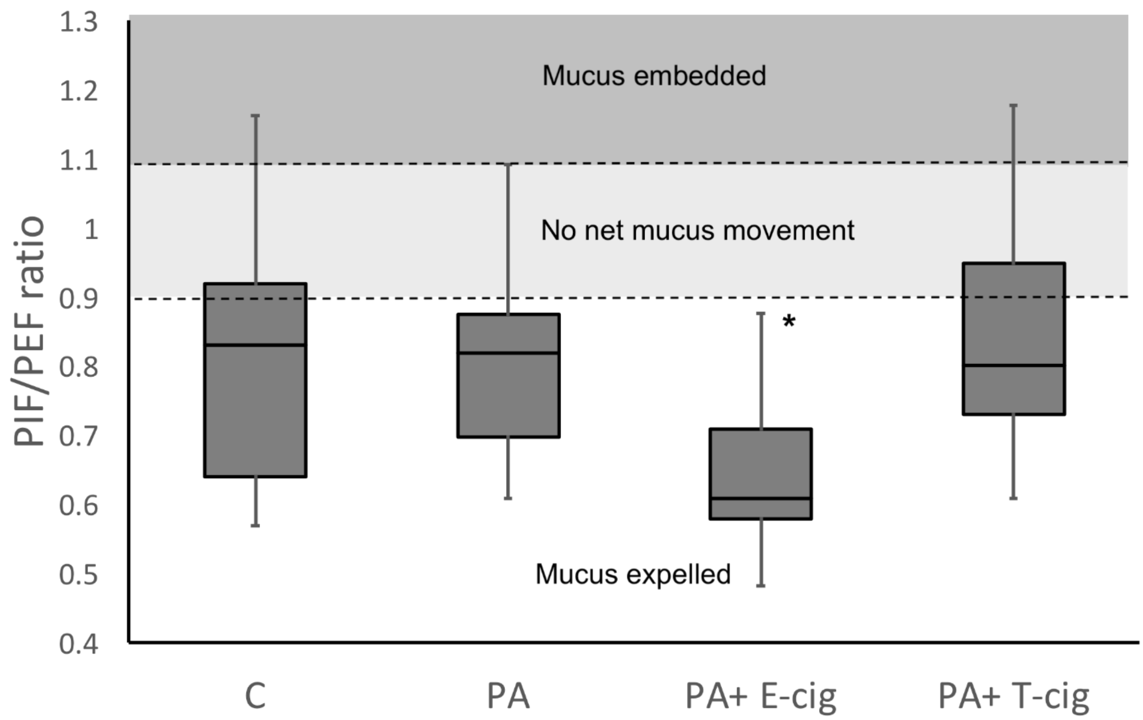

Fig. 3 PIF/PEF ratio
* statistically significant difference between PA+ e-cig and other groups; different colour areas represent movement of mucosa (Ntoumenopoulos et al., 2011).

Discussion

The main results of our study are as follows: Firstly, physically active non-smokers have statistically higher respiratory flows compared to other groups. Additionally, e-cigarette smokers have significantly lower inspiratory flows compared to all other groups. Secondly, all groups exhibit normal lung resistance; however, tobacco smokers have a statistically significantly higher resistance compared to e-cigarette smokers. Thirdly, physically active males who smoke e-cigarettes have a smaller PIF/PEF ratio, indicating enhanced additional clearance due to mechanically stimulated airway flow.

In healthy, physically active young males, smoking significantly decreases the forced vital capacity (FVC) and forced expiratory volume in the first second (FEV_1) (Table 1) compared to non-smoking counterparts. It is known that adequate and good lung function indicates lung capacity that requires full diaphragmatic work (Grams et al., 2012), so we could speculate that one of the mechanisms by which smoking exerts its influence is the reduction of respiratory muscle work. Especially decreased PIF values, which were significantly lower in the e-cigarette smoking group (Table 1), correlate with decreased inspiratory muscle strength (Leving et al., 2022). The deficiency in antioxidants as a consequence of smoking and the body's inability to defend itself against the destructive effects of oxidative radicals (Weiss, 2021) can decrease muscle's ability to generate larger forces, which are needed for deep forced respiration. However, the reduction in lung capacities was still within the physiological norm, making lung functionality similar to that of non-physically active individuals (Table 1).

Previous research suggests that forced expiratory flows such as $FEF_{25\text{-}75\%}$ or $FEF_{25\text{-}50\%}$ are more sensitive indicators than FEV_1 for detecting obstructive small airway disease (Simon et al., 2010; Ciprandi, Cirillo, 2011). Furthermore, forced flow parameters like $FEF_{25\text{-}75\%}$ can predict the development of chronic obstructive pulmonary disease (COPD) in patients with normal lung function (Kwon et al., 2020). In our study, forced expiratory flows (Table 1) were significantly higher in physically active non-smokers (PA) compared to non-physically active (C) or physically active smoker groups (PA+e-cig or PA+t-cig).

Smoking intensity, regardless of age, is known to be a significant factor in the decline of airway-specific conductance and the increase of residual volume (Nagelmann et al., 2011). One parameter that can indicate changes in airway resistance is the expiratory time constant (RC_{EXP}). This parameter allows us to assess respiratory mechanics and characterize lung compliance. Lung function deviation and structural changes are present in chronic smokers before the clinical signs of airway obstruction (Nagelmann et al., 2011). Our results (Figure 2) showed that all groups had acceptable RC_{EXP} values, aligning with findings that most patients without airway obstruction have an RC_{EXP} shorter than 0.6 seconds (Ikeda et al., 2019) and an average time constant of 0.38 seconds (ranging from 0.28 to 0.51 seconds) in healthy, non-intubated subjects (McIlroy et al., 1963). Accordingly, an RC_{EXP} greater than 0.7 seconds indicates an increase in lung resistance (Eghtedari et al., 2021). The only significant difference (Figure 2) was between smoking groups, indicating a much smaller RC_{EXP} in e-cigarette smokers compared to tobacco smokers. Furthermore, e-cigarettes are associated with an increased risk of respiratory symptoms among never-smoking youth and non-daily ever cigarette smokers (Chaiton et al., 2023).

Interestingly, one factor that could be influenced by smoking in the respiratory system without physically changing the respiratory system is airway clearance. Airway clearance includes mechanisms of respiratory epithelium ciliary movement, mucosa production, and airway surface hydration by mechanical deformation of the airway surface (Randell et al., 2006) and movement of flow (Kim et al., 1987), which can be evaluated by spirometry (Ntoumenopoulos et al., 2011). According to Ntoumenopoulos and co-authors (Ntoumenopoulos et al., 2011), the PIF/PEF ratio can show the airflow-induced mechanical clearance of the respiratory system, favouring cephalad mucus movement or accumulation according to respiratory flow rates. It has been reported that to move mucus cephalad, the PEF must exceed PIF by 10% (PEF/PIF > 1.1), creating an expiratory flow bias (Pursley, 2017-2018). According to this evaluation, all groups had cephalad clearance; however, the e-cigarette smoking group had a significantly lower ratio (Figure 3). We speculate that this is more likely related to the group's significantly lower PIF values (Table 1) rather than a physiological need for increased sputum and mucus transportation, as all our subjects did not exhibit any respiratory symptoms. It is known that lower PIF correlates with decreased handgrip strength, inspiratory muscle strength, and disease characteristics like lung hyperinflation (Leving et al., 2022). This aligns with our finding that the $PIF/FEF_{50\%}$ ratio was lower in the e-cigarette smoking group (Table 1), a pattern previously reported to be associated with changes in bronchial asthma but not seen in COPD (Okazawa et al., 2020).

The study limitations are primarily related to the sample. Firstly, the gender; all participants in our study were male. Since gender influences some respiratory parameters and their norms (e.g., FVC, flows, etc.) and the respiratory system's adaptation (LoMauro, Aliverti, 2021), this could affect the study outcomes. Secondly, the sample size; each group had around 20 participants. This number needs to be increased for generalization to the larger population. Thirdly, physical activity was self-reported, and no functional tests such as VO_{2max} or PWC_{170}, which can indicate an individual's level of fitness, were used. Lastly, voluntary spirometry was used to record data. Since this method heavily relies on the participant's effort, it can introduce some recording errors. However, to minimize this error, our study utilized repeated measures with three recordings.

Conclusions

In conclusion, physical activity partially blunts the changes of the respiratory system caused by at least two years of e-cigarettes or tobacco cigarettes smoking.

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