# Smoking Pattern in Men and Women: A Possible Contributor to Gender Differences in Smoke-related Lung Diseases

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## INTRODUCTION

Chronic obstructive pulmonary disease (COPD) due to cigarette smoking is a major cause of morbidity and mortality worldwide. Given the same amount of exposure to tobacco smoke, women are more likely to develop more severe airflow limitation at an earlier age than men(1). Importantly, at all stages of COPD severity, men have a more severe computed tomography (CT)-defined emphysema than women(2). Also, the prevalence odds ratio (OR) for screen-detectable lung cancer (conditional on age and smoking history) indicates that women have an increased susceptibility to tobacco carcinogens but have a lower rate of fatal outcome of lung cancer compared with men(3).

So far, the reasons why women differ from men in cigarette smoking susceptibility and the pathological and clinical expressions of COPD, remain largely unknown. Higher levels of cigarette smoke metabolites, such as polycyclic aromatic hydrocarbons adducts, have been previously found in the lungs of women smokers compared to men (4). Thus, we hypothesize that the differences in the way women and men inhale smoke from cigarettes may, at least in part, contribute to the different clinical and pathological COPD clinical and disease phenotypes between genders. Using Optoelectronic Plethysmography (OEP), a non-invasive motion capture method to measure chest wall movements and estimate lung volumes, we assessed the smoking pattern of a matched woman and man population.

## METHODS

Twenty-eight active smokers, 14 men and 14 women, matched by anthropomorphic data and smoking habit, and free of pulmonary and other relevant diseases and not under chronic medical treatment, were recruited (see **Table 1**). First, the breathing pattern during ten consecutive tidal breaths was assessed. Then, the subjects were invited to puff a cigarette with filter mimicking the way they usually smoke, including the depth of the puff (puff volume), the duration of the puff, and the interval between puffs. In order to standardize the procedure of data collection, after ignition of the cigarette the first 5 puffs were excluded in order to allow the subject to stabilize his/her puffing pattern. Then, the volume of the following 5 puffs was measured by OEP. Moreover, in order to standardize the breathing frequency and to avoid confounding effects on total and compartmental tidal volumes,

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we excluded the subjects with a smoking puff time more than 1.5 seconds with a smoking volume greater than 30% of the vital capacity (VC). A dedicated software computed the enclosed volume and its variations during breathing with high accuracy, providing a measurement of the three-dimensional micro-movement of the points belonging to the chest wall to compute volume variations of the whole chest wall and the different compartments(5): pulmonary rib cage (RCp), abdominal rib cage (RCa), and the abdomen (Abd). The measurement of the volumes of each hemithorax was provided by midline sensors (anteriorly, along the sternum and continuing caudally below the xiphoid through the umbilicus, and posteriorly, along the spinous processes of the vertebral column).

The software takes into account three main factors: 1) the lung- and diaphragm-apposed parts of the rib cage (RCp and RCa, respectively) are exposed to substantially different pressures on their inner surface during inspiration; 2) the diaphragm acts directly only on RCa; and 3) non-diaphragmatic inspiratory muscles act largely on RCp. Abd volume change is defined as the volume swept by the abdominal wall (**Figure 1**).

**RESULTS**

Men and women had similar anthropometric data and pulmonary function (**Table 1**). During tidal breathing, both men and women mainly recruited the RCp compartment, to a lesser extent the Abd, and minimally the RCa. The inhaled cigarette smoke volume (25 ± 3 % VC in men and 24 ± 3 % VC in women; p= 0.352) and the smoke inhalation time (1.1 ± 0.2 seconds in men and 1.0 ± 0.2 seconds in women; p= 0.533) were similar between men and women. The compartmental distributions of the smoking volume in the three compartments (pRC, aRC, and Abd) between right vs. left hemithoraces within women and men, and between women vs. men are shown in **Table 2**.

Instead, the smoke inhalation volume, in each right and left hemithoraces, was mainly concentrating in the RCp and Abd compartments, in men. In women, 58% and 54% (right and left side, respectively) of the total smoke inhalation volume was concentrated in the RCp, whereas the remaining volume was distributed between RCa and Abd. This difference in distribution between

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men and women was emphasized by averaging up both hemithoraces. In men, RCp and Abd shared almost 80% of the smoke inhalation volume (RCp vs RCa: $p<0.0001$; Abd vs RCa: $p<0.001$; RCp vs Abd: N.S.), whereas in women the smoke inhalation volume was mainly collected in RCp (RCp vs RCa: $p<0.0001$; RCp vs Abd: $p<0.0001$; Abd vs RCa: $p<0.05$). The smoking volume collected in RCp and Abs was significantly different between men and women (Table within **Figure 1**).

**DISCUSSION**

We show for the first time that, while smoking, women preferentially recruit the rib cage with lesser contribution of the abdomen, whereas men preferentially recruit the abdominal compartment. This may be one potential mechanism contributing to the different cigarette smoke susceptibility, and the incidence of lung cancer and COPD, observed between women and men.

Women smokers develop more airflow limitation and more severe COPD, despite lower exposure to tobacco(2), and have a more rapid annual decline in $FEV_1$ than men smokers, even when they smoke fewer cigarettes(6). Furthermore, women with severe COPD have a higher risk of hospitalization and death from respiratory failure and comorbidities(7). However, the underlying reasons are largely unknown.

The different susceptibility to tobacco smoke could reflect a gender difference in the metabolism of cigarette smoke or in the inflammatory response to cigarette smoking due to hormonal effects(8). We are now adding another mechanism potentially associated with the increased susceptibility to cigarette smoke observed in women: how cigarette smoke is inhaled and distributes throughout the lung.

At birth, the lungs of women are on average smaller than those of men, and have fewer respiratory bronchioles. The airways in women are relatively smaller than those in men for the same lung volume, so there may be a higher concentration of tobacco smoke per unit area(9). During the growth, the development of new lung parenchyma and airways, and the loss of lung elastic recoil, occur in women earlier than men(10). However, this maturation process occurs homogeneously throughout the lung and

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it is unlikely associated with the difference in the smoking pattern that we observe between men and women.

One possible explanation to our findings is that, during the biological evolution of the human species, an adaptation of the respiratory system anatomy in the women occurred, to allow the gravid uterus to grow the fetus. This possible adaptation might underlie the predominant recruits of the upper areas of the thorax in women while enhanced breathing (smoking). As our data are observational we cannot provide evidence to support mechanisms underlying the gender differences in the smoking pattern observed in our study. However, it is important to note that, in our case study there were not only women who had had at least one pregnancy but also women who had never given birth, and the compartmental smoking distribution between them was similar.

To our knowledge, there are no other described physiological conditions where women use the rib cage compartment more than men. Interestingly, it has been previously demonstrated, by using chest radiographs, that women exhibit a greater inspiratory rib cage muscle contribution and volume expansion during resting breathing than men, presumably reflecting an improved mechanical advantage conferred to these muscles by the greater inclination of ribs (11).

Limitations of the study include the observational nature of the study and the fact that we did not confirm the spatial distribution of the inhaled cigarette smoke by using a tracer. However, OEP is an excellent non-invasive tool to determine compartmental displacement during breathing accurately, and has the advantage of allowing accurate observation without complex instrument interference.

To conclude, we show for the first time that, while smoking, women mainly engage the pulmonary ribcage, whereas men mainly engage the abdominal compartment. These findings may help explain the increased susceptibility to cigarette smoke in women vs. men, which underlies the increased risk of developing COPD, severe emphysema, and lung cancer in the woman population.

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## FIGURE LEGEND

**Figure 1**: Optoelectronic Plethysmography configuration of infrared-reflective markers identifying three main compartments associated with breathing: Blue= pulmonary rib cage, RCp; Green= abdominal rib cage, RCa; Yellow= abdomen, Abd. Left microphotograph: anterior view; Middle microphotograph: lateral view; Right microphotograph: posterior view.

Table: Pairwise comparison (Student t-test) of the total smoking volume distribution in men and women in the three thoracic compartments.

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## TABLES

**Table 1**: Baseline characteristics of the study population. Statistical analyses included one-way analysis of variance tests for continuous variables, followed by pairwise comparisons using Student's t tests or Mann-Whitney U tests. Pairwise comparisons showed no significant differences in the percentage of men, ages, pack/years, pulmonary function, and anthropometric data, between men and women. Data are presented as mean ± SD. BMI: body mass index; $FEV_1$: forced expiratory volume in one second; FVC: forced vital capacity; ITGV: inspiratory thoracic gas volume. TLC: total lung capacity. SmoV: smoking volume. SmoIT: smoking inhalation time

| **Variable** | **Women** n=14 | **Men** n=14 | ***P-value*** |
|---|---|---|---|
| Age | 46±11 | 41±9 | 0.182 |
| Height (m) | 167±5 | 167±5 | 0.944 |
| Weight (Kg) | 67±7 | 70±8 | 0.381 |
| BMI ($Kg/m^2$) | 24±3 | 25±3 | 0.420 |
| Pack-yrs | 23±8 | 25±9 | 0.464 |
| $FEV_1$ (% pred.) | 101±9 | 104±8 | 0.371 |
| FVC (% pred.) | 107±8 | 103±7 | 0.232 |
| $FEV_1$/FVC (% pred.) | 107±0.2 | 112± 0.2 | 0.533 |
| ITGV (% pred.) | 118±11 | 112±19 | 0.244 |
| TLC (% pred.) | 106±14 | 99±10 | 0.142 |
| SmoV (% VC) | 24±3 | 25±3 | 0.352 |
| SmoIT (sec) | 1.0±0.2 | 1.1±0.2 | 0.533 |

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## Table 2.

**Table 2A:** Differences in the smoking volume distributions, expressed as percentage of the total smoking volume puff (% SmoV), in each compartment (pulmonary rib cage= RCp, abdominal rib cage= RCa, abdomen= Abd), between right vs. left side in women and men.

**Table 2B:** Differences in % SmoV distribution in each compartment (RCp, RCa, Abd) in the right and left sides between women vs. men.

| **2A** | **Within Men** | | | **Within Women** | | | **2B** | **Men vs. Women** | |
|---|---|---|---|---|---|---|---|---|---|
| | % SmoV R side | % SmoV L side | ***P value*** | % SmoV R side | % SmoV L side | ***P value*** | | % SmoV R sides | % SmoV L sides |
| **RCp** | 21 ± 7 | 20 ± 7 | 0.62 | 30 ± 6 | 26 ± 6 | 0.15 | | ***P value*** | |
| **RCa** | 10 ± 4 | 11 ± 3 | 0.40 | 9 ±2 | 10 ± 4 | 0.80 | **RCp** | **0.001** | **0.010** |
| **Abd** | 19 ± 6 | 19 ± 8 | 0.87 | 12 ±6 | 13 ± 7 | 0.68 | **RCa** | 0.473 | 0.201 |
| **Total** | 100 | | | 100 | | | **Abd** | **0.001** | **0.038** |

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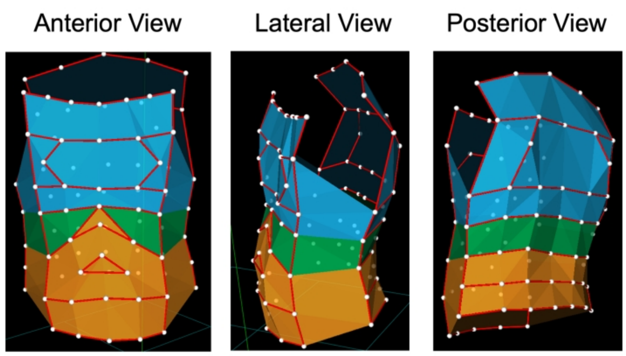


| | Males | Females | *P Value* |
|---|---|---|---|
| RCp | 40 ± 13 | 56 ± 10 | 0.0001 |
| RCa | 22 ± 6 | 19 ± 4 | N.S |
| Abd | 38 ± 13 | 25 ± 9 | 0.02 |

Figure 1

338x190mm (225 x 225 DPI)

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