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Correlation Between Impulse Oscillometry and Spirometry in Assessment Of Small Airway Dysfunction In Asymptomatic Smokers

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Background: The traditional pulmonary function tests may be inadequate to detect Chronic Obstructive Pulmonary Disease (COPD) pathological damage and smoking-related lung disease. An impulse oscillation system (IOS) is a novel method for reactance and airway resistance measurements. It is a kind of forced oscillation, where sound waves oscillate at different frequencies, usually between 5 and 20 Hz, and propagate through the bronchial tree. It measures the proximal airway resistance (measured at 20 Hz [R20]), the peripheral airway resistance (measured at R5–R20), and the overall airway resistance (measured at 5 Hz [R5]). Resistance and reactance make up impedance. IOS provides more detailed information than spirometry on regional lung function and should be considered as being complementary to spirometry to comprehensively assess lung function in COPD.

Objectives: The objective of our study is to assess the correlation between impulse oscillometry and spirometry parameters in small airway dysfunction in asymptomatic smokers in a tertiary care centre; and to determine the association of smoking index with impulse oscillometry small airway dysfunction parameter R5-R20.

Materials And Methods: The study was conducted in the Department of Pulmonary Medicine, Medical College Hospital, Thiruvananthapuram. The present cross-sectional study included asymptomatic current smokers, eligible participants underwent spirometry and oscillometry and the results were compared.

Results: Out of 45 patients studied, 44.4% (n=20), fell within the 45-60 age range. The majority of participants, comprising 37.8% (n=17), had a Smoking Index ranging from 300 to 399. Correlation analysis between FEF (25-75) vs (R5-R20) done by Pearson correlation test reported a very mild negative correlation between them (r=-0.053, p=0.728). The chi-square test reported a significant association between smoking index & R5-R20 ($p<0.05$).

Conclusion: Impulse oscillometry is capable of detecting SAD in asymptomatic smokers with preserved spirometry and with FEF(25-75) values in the normal range. We verify that IOS offers parameters that can contribute to conventional pulmonary function tests.

Keywords: Forced oscillation technique, spirometry, resistance, reactance, small airway dysfunction, impulse oscillometry, forced expiratory flow (25–75%), smoking index

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Introduction

One of the main causes of illness and death globally is a chronic obstructive pulmonary disease, or COPD. The World Health Organization (WHO) estimates that COPD-related causes of death account for 3 million deaths worldwide annually. Precise diagnosis of COPD and close observation of treatment response are especially crucial. When combined with appropriate counselling and quitting smoking, small airway dysfunction, if identified early, may help stop the disease's progression. [1]

The Global Initiative for Obstructive Lung Disease (GOLD) guidelines state that the ratio of forced expiratory volume in 1 second (FEV1)/forced vital capacity (FVC) <70% after bronchodilator inhalation is an essential criterion for the diagnosis of COPD. PFTs are the gold standard for diagnosis.[2] Routine PFTs are particularly challenging for older patients, those with poor motor coordination, deficits in cognition, and respiratory problems, especially when it comes to the evaluation of FVC.[3]

The conventional pulmonary function parameter, FEV1, is crucial for the diagnosis of COPD and aids in the evaluation of airflow limitation. It may not fully reflect the clinical alterations, though, and is not sensitive to peripheral airway obstruction. Forced expiratory flow (25–75%) (FEF25–75) is the average flow from the point at which 25% of the FVC has been exhaled to the point at which 75% of the FVC has been exhaled. It is defined as forced expiratory flow over the middle one-half of the FVC. [4]

Using noninvasive pressure fluctuations superimposed on the airway over the subject's normal, quiet tidal breathing, airway mechanics could be measured, known by the broad term "forced oscillation technique" (FOT), which was first found by Dubois et al. more than 50 years ago. FOT includes impulse oscillometry (IOS) as a subtype. To evaluate the mechanical properties of the upper and intrathoracic airways, lung tissue, and chest wall during tidal breathing, it provides an oscillating pressure signal—also referred to as an input or forcing signal—to the respiratory system, typically at the mouth. [5]

An impulse oscillation system (IOS) is a novel method for reactance and airway resistance measurements. It is a kind of forced oscillation [6], where sound waves oscillate at different frequencies, usually between 5 and 20 Hz, and propagate through the bronchial tree. It measures the proximal airway resistance (measured at 20 Hz [R20]), the peripheral airway resistance (measured at R5–R20), and the overall airway resistance (measured at 5 Hz [R5]). Resistance and reactance make up impedance. Resistance is the part of lung impedance that aligns with the airflow pressure in the conducting airways, while reactance is the part that is out of sync with the airflow pressure and indicates the airways' capacitive and inertive properties. Reactance consists of both elastance (or capacitance) and inertance. Respiratory system elastance (Ers) measures the overall stiffness of the respiratory system, encompassing the chest wall, lungs, and airway walls. It also reflects the compressibility of gases in the alveoli and airways at oscillometry frequencies. Ers is inversely related to the concept of compliance. When volume changes occur, the elastic forces cause a delay in pressure changes relative to flow changes, leading to a negative reactance.

Pressure loss due to capacitance is more significant than pressure loss due to inertance at low frequencies, whereas at higher frequencies, inertive properties become more dominant. Capacitance represents the elasticity of the airways, while inertance relates to the mass-inertive forces of the moving air column. Reactance can be understood as the rebound resistance, offering insights into the distensibility of the airways. The physical properties of the lung parenchyma, including its ability to expand and facilitate alveolar filling, are associated with reactance measured at 5 Hz (X5). When capacitance and inertance forces are balanced, reactance reaches zero, known as the resonant frequency (Fres). The respiratory reactance between 5 Hz and the resonant frequency is represented by the reactance area (Ax), which sums up all the reactance values from X5 to the resonant frequency. [7] In this context, this study aims to assess small airway dysfunction using IOS.

Objectives

Primary Objective: To assess the correlation between impulse oscillometry and spirometry parameters in small airway dysfunction in asymptomatic smokers in a tertiary care centre.

Secondary Objective: To determine the association of the smoking index with impulse oscillometry parameter R5-R20.

Methodology

Study Design: Cross-sectional study

Study Setting: The study was conducted in the Department of Pulmonary Medicine, Govt. Medical College, Thiruvananthapuram.

Study Period: One and half years after getting Institutional Ethical Committee clearance.

Study Population: Bystanders of patients admitted/visiting OPD, in the Pulmonary Medicine Department, Medical College Hospital, Thiruvananthapuram, who are current smokers having smoked at least 100 cigarettes.

Inclusion Criteria: Participants who gave consent, aged >18 years, current smokers (who have smoked at least 100 cigarettes in their lifetime and have smoked within the past year), who had no symptoms of cough, phlegm or shortness of breath, explained by smoking.

Exclusion Criteria: Patients with cardiac diseases, previous history of pulmonary tuberculosis, history of asthma, current smokers with reduced FVC (<80% predicted) or FEV1/FVC ratio <0.7, those with IOS coherence value <0.8.

Sample Size:

The sample size was estimated using the formula

$$\frac{\left(Z_{(1-\beta)}+Z_{\left(1-\frac{\alpha}{2}\right)}\right)^2}{\left(\frac{r^2}{1-r^2}\right)}$$

If power is 90% then $Z_{(1-\beta)}$ will be 1.282

$Z_{(1-\alpha/2)}$ is 1.96

R is the correlation coefficient.

In the study by Xia Wei, Zhihong Shi et al: r value is -0.452

$$N = \frac{(1.282+1.96)^2}{\left(\frac{0.452^2}{1-0.452^2}\right)} = \frac{10.510}{0.221} = 41$$

The sample size was taken as 45.

Sampling Method: Eligible participants were selected consecutively till the sample size was reached.

Study Variables:

A) Demographic variables:

1) Age:
2) Sex:
3) Occupational exposure:
4) Smoking index:
5) BMI :
6) Education:
7) Income
8) Urban/rural dwelling:

B) Disease variables:

- Spirometric indices like FVC, FEV1, FEV1/FVC, FEF(25-75).
- Impulse oscillometry indices like Resistance at 5Hz (R5), at 20HZ (R20), R5-R20, Reactance at 5 Hz (X5).

Data Collection Tools and Technique:

Data was collected in a semi-structured questionnaire.

- Informed consent was obtained from those accompanying patients (may or may not be a blood relative) admitted to the pulmonary medicine ward or attending pulmonary medicine OPD at medical college hospital Trivandrum, who were current smokers without any respiratory symptoms. Spirometry was performed on all subjects, and smokers were advised to abstain for at least one hour before testing.

Ethical Considerations:

- Informed written consent was obtained from all participants.
- Subject confidentiality was upheld throughout the investigation.
- No financial burden was imposed on subjects.
- The institutional review board and human ethics committee clearance were required before the study could begin.

Results

The distribution of participants according to their R5-R20 values is shown below, They were divided into two groups according to their R5-R20 values: ≤1 and >1 cmH2O/L/s. 73.3% (n=33), exhibited an R5-R20 value exceeding 1 indicative of small airway dysfunction.

Table 1: R5-R20

		Frequency	Percent
R5-R20 (cmH2O/L/s)	≤1	12	26.7
	>1	33	73.3
	Total	45	100.0

Table 2: FEF (25-75%)

		Frequency	Percent
FEF (25-75%) (% predicted)	<65	24	53.3
	>65	21	46.7
	Total	45	100.0

The participants are distributed according to their Forced Expiratory Flow (FEF) between 25% and 75% of their forced vital capacity (FVC), which is referred to as FEF (25-75%). Approximately 53.3% (24 individuals) of participants had an FEF (25-75) value below 65, indicating airflow limitation in small airways within this subgroup.

Table 3: Correlation of FEF(25-75) & R5-R20

		R5-R20
FEF(25-75)	Pearson Correlation	-0.053
	Sig. (2-tailed)	0.728
	N	45

P<0.05 is statistically significant.

Correlation analysis between FEF (25-75) vs (R5-R20) was done by Pearson correlation test and reported a very mild negative correlation between them (r=-0.053, p=0.728).

Table 4: Association table between Smoking index & R5-R20

			R5-R20		Total	P VALUE
			≤1	>1		
smoking index	200-299	Count	8	2	10	0.0001 *
		% within the smoking index	80.0%	20.0%	100.0%	
	300-399	Count	4	13	17	
		% within the smoking index	23.5%	76.5%	100.0%	
	400-499	Count	0	14	14	
		% within a smoking index	0.0%	100.0%	100.0%	
	500-599	Count	0	3	3	
		% within a smoking index	0.0%	100.0%	100.0%	
	>599	Count	0	1	1	
		% within a smoking index	0.0%	100.0%	100.0%	
Total		Count	12	33	45	
		% within a smoking index	26.7%	73.3%	100.0%	

P<0.05 is statistically significant.

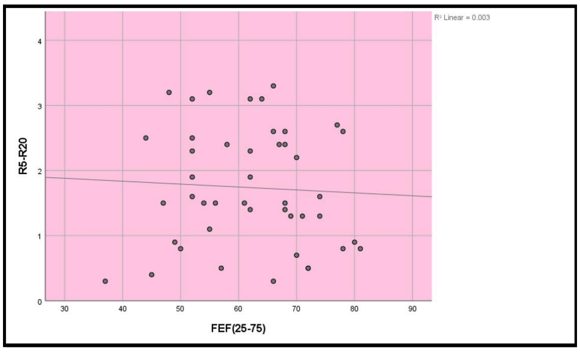

Figure 1: Correlation of FEF(25-75) & R5-R20

The chi-square test reported a significant association between smoking index & R5-R20 (p<0.05).

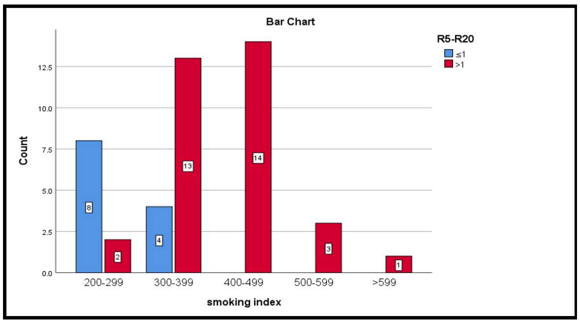

Figure 2: Association table between IOS & spirometry

Discussion

Obstructive lung diseases often manifest by small airway obstruction. Little is known about small airway obstruction, its prevalence, and risk factors worldwide. The recognition of a substantial small airway obstruction burden in multiple geographical locations bears significant implications for global health, particularly considering the possibility that isolated small airway obstruction could serve as a predictive marker for the development of obstructive lung disease in the future.

Future research, especially in individuals whose lung function is generally normal, may establish a connection between small airway obstruction and both an elevated burden of symptoms and an abrupt decline in lung function.[9][10] From the literature search, there was disagreement over the diagnostic criteria, with both the lower limit of normal and percent predicted cutoffs being used.

For small airways, most population-based research used the forced expiratory flow rate (FEF25–75), which ranges from 25% to 75% of the forced vital capacity. Few studies in the literature have addressed the frequency of small airway disease as a primary outcome. The prevalence varied depending on the world region and spirometry parameter selected, ranging from 7.5% to 45.9%. Two population-based studies, both in China, [8] [14] identified several risk factors for small airway obstruction, including passive smoke exposure, smoking, low body mass index, ageing, female sex, use of solid fuels for cooking or heating, low level of education, and a family history of COPD. Depending on the spirometry parameter utilized, prevalence estimates and associations can change. Given its link to forced vital capacity, it is probable that FEF(25–75) is inappropriate as a binary measure to categorize the presence of small airway obstruction, though further study is required in this area. [9]

Prior studies demonstrated that spirometry was less sensitive than IOS in identifying small and large airway dysfunction in a variety of clinical and research contexts. [11] [15] IOS was more sensitive in identifying SAD and linked better with symptoms than spirometry in participants with persistent respiratory symptoms and normal spirometry. [12] We have tried to explore the utility of IOS to detect early changes in small airways which may remain asymptomatic. Modifiable risk factors, especially smoking, are often overlooked early on by smokers without apparent health issues and many continue to smoke habitually. We tried to demonstrate the hidden risk of smoking in the development of SAD in asymptomatic smokers as well as to stress the need to quit smoking to prevent disease progression.

Our study included 45 subjects, all males, with the majority (44.4%) aged between 45-60 years, followed by 30-44 years (28.9%). 73.3% (n=33), fell within the BMI range of 18.5-22.9kg/m². 37.8% (n=17), had a smoking index ranging from 300 to 399. The second largest group, representing 31.1% (n=14), fell within the range of 400 to 499. 55.6% (n=25) subjects had FEV1/FVC ratio of 0.7-0.79. The study by Roberta Pisi, et.al, had 75 asymptomatic smokers (including 37 females) with a mean age of 47±12 years and 26±17 pack-years. In our study, spirometry showed FEF (25-75%) <65% predicted in 53.3% (n=24) implying SAD whereas IOS showed R5-R20 value of >1cmH_2O/L/s in 73.3% of subjects.

There was a negative correlation between FEF (25-75) and R5-R20 which was not statistically significant (p=0.728, r=-0.053). Of the 24 subjects with SAD in spirometry, IOS showed SAD in 70.8% (n=17), normal values in 16.6% (n=4), large airway obstruction in 4.1% and combined airway obstruction in 8.3%. Similarly, out of 21 subjects without SAD in spirometry, IOS detected the same in 66.6% (n=14). There was no significant association seen between spirometry and IOS (p=0.27).

The study by Roberta Pisi, et.al. found that smokers with at least 30 pack-years were aged 53±10 years, with a BMI of 27±4 kg/m². In all smokers, pack years were significantly related to spirometry and IOS parameters (p<0.05). 14.6% of smokers showed SAD in IOS and 5.3% of smokers showed SAD in spirometry. There was a direct significant correlation between pack years and BMI. In our study, there was a significant association between smoking index & R5-R20 (p=0.0001). All the participants with a smoking index >400 (40%) had evidence of small airway dysfunction on IOS. While 76.5% with a smoking index between 300-399 had SAD, 20% had SAD with a smoking index between 200-299. No significant association was found between the smoking index and spirometry parameter FEF (25-75%) (p=0.119). There was no significant association between R5-R20 and BMI in our study (p=0.36).

In another cross-sectional observational study conducted in China by JieqiPeng,FanWu, et.al, the prevalence of IOS-SAD in the total cohort was 32.9% (437/1327), with most of them between 60-69 years of age, with 30 to 44 and more than 45 pack-years. The mean BMI did not significantly differ between the non-SAD group and the IOS-SAD group (22.8 ± 3.1 vs. 22.9 ± 3.7 kg/m² (p = 0.89).

The study by K Malu, J Mullerpattan, et.al. [13] was a prospective, cross-sectional study which assessed the IOS results in 102 subjects with preserved spirometry and its correlation to smoking status. It included 51 current or former smokers (>10 pack years history) and 51 non-smokers. The mean age was 49 years with male predominance (77.5%). Smokers had a significantly higher incidence of SAD on IOS despite preserved spirometry (p=0.005). Higher pack year history correlated significantly with the development of SAD (p=0.0001).

The study by Al-Mutairi et al. reported in 2007 that the sensitivity of IOS for asthma was 31.3%, while the sensitivity of conventional pulmonary function tests was 19.6%. They found that the sensitivity of IOS in COPD was 38.95%, while the sensitivity of conventional pulmonary function tests was 47.4%. When it came to identifying healthy individuals, IOS's sensitivity of 45.8% outperformed PFT's (28.8%). IOS and conventional PFT have 80.5% and 86.2% specificity, respectively, in identifying healthy individuals. [16] This suggested that when diagnosing mild COPD and assessing modest airway alterations following bronchodilator and bronchoprovocation challenges, IOS resistance measurements can be helpful. [17]

Using various IOS parameters, Winkler et al. identified 87–94% of patients with COPD and asthma. [18] Even though many studies have focused on the usefulness of IOS, there is very limited research on asymptomatic individuals to detect SAD early before progression to established disease.

Conclusion

Impulse oscillometry is capable of detecting SAD in asymptomatic smokers with preserved spirometry and with FEF(25-75%) values in the normal range. We verify that IOS offers parameters that can contribute to conventional pulmonary function tests. Further research is necessary to examine the connection between SAD, as determined by IOS, and the onset of COPD. To achieve IOS reference values, extensive research on normal, healthy population samples is required.

Limitations

As there are currently no widely acknowledged normal reference values for the IOS measurement, we used the absolute values rather than those expressed as a percentage of the predicted value. Since this study is cross-sectional, there is no follow-up of those with SAD to look for COPD.

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