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Coexistence of upper airway obstruction on spirometry with flow volume loop in patients with chronic obstructive pulmonary disease

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Abstract

Chronic obstructive pulmonary disease (COPD) can arise from smoking and non-smoking causes. Spirometry with flow–volume loop (FVL) analysis is a simple and essential test not only for diagnosing COPD but also for detecting upper airway obstruction (UAO). Identifying the coexistence of UAO in COPD has important clinical implications. The present study was an independent analysis of spirometry data from COPD patients (ECARP/2022/124) over 2 years at a tertiary care center. Various spirometry parameters and FVL patterns were assessed, including visual loop flattening, forced expiratory flow at 50% of vital capacity, forced inspiratory flow at 50% of vital capacity ratio (FEF50/FIF50), FIF50, and Empey's index. Patients meeting 3 of 4 standard UAO criteria were classified as having UAO.

A total of 193 COPD patients were included (mean age 56.3 years). Visual loop flattening was observed in 27% (7% inspiratory, 20% expiratory). The FEF50/FIF50 ratio was >1 in 17% and <0.3 in 44%, suggesting variable intrathoracic obstruction as the most common type of UAO. FIF50 <100 L/min was noted at 27.3%. Overall, 7.21% of patients met 3 of 4 diagnostic criteria for UAO.

Thus, a significant subset of COPD patients demonstrated features of coexisting UAO. Routine spirometry with FVL analysis provides a valuable, noninvasive tool to identify this overlap, which may influence diagnosis, management, and patient outcomes.

Key words: UAO, COPD, spirometry, flow volume loop, Empey's index, FEF50/FIF50 ratio, FIF50.

Introduction

Chronic airway disease (CAD), which includes conditions like Chronic obstructive pulmonary disease (COPD), bronchial asthma, bronchiectasis, and obliterative bronchiolitis (OB), are a major contributor to respiratory-related morbidity and mortality [1]. COPD is a common but underrecognized condition and the only chronic disease with a steady rise in prevalence over the past 50 years. It now stands as the third leading cause of death worldwide, affecting over 400 million people [2].The 2023 Global Initiative for Chronic Obstructive Lung Disease (GOLD) update redefined COPD and introduced a new taxonomy based on etiotypes: genetically determined (COPD-G), abnormal lung development (COPD-D), smoking-related (COPD-C), infection-related (COPD-I), pollution/environmental exposure (COPD-P), and unknown cause (COPD-U) [3]. A key feature of COPD is poorly reversible airway obstruction, mainly due to pathological changes in small airways (<2 mm). Their loss and narrowing increases the peripheral resistance and cause dynamic airway collapse during expiration, leading to airflow limitation [4]. The upper and lower airways form a continuous, integrated unit with similar responses to noxious stimuli [5]. The upper airway (UA) extends from the mouth up to the cricothyroid cartilage in the respiratory tract [6]. Upper airway obstructions (UAO) can be defined as decrease in diameter of larynx, extra thoracic or intrathoracic trachea, and main bronchi, presenting acutely or chronically based on the underlying etiology and type of obstruction. It is classified as variable UAO, if obstruction changes with respiration, or fixed UAO if site of obstruction remains constant. Variable UAO is further subdivided into variable extra thoracic upper airway obstruction (VET UAO) and variable intrathoracic upper airway obstruction (VIT UAO) [7]. Spirometry with flow–volume loop (FVL) is a valuable, non-invasive tool for detecting upper airway obstruction (UAO), often revealing early morphological changes before standard spirometry[7]. COPD dynamically involves small and large airways hence UAO may coexist. When both are present, it becomes difficult to determine each condition's contribution to respiratory impairment using only clinical evaluation, imaging, or standard pulmonary function tests alone [8]. This study focuses on utilizing spirometry to identify the coexistence of UAO in COPD and assess its impact on lung function. While laryngoscopy and bronchoscopy is the diagnostic gold standard, FVL offers a practical screening alternative. This study aims to assess the presence and features of UAO in COPD patients using FVL, highlighting the importance of early detection to improve outcomes and reduce healthcare burden.

Materials and Methods

This independent subset analysis focused on spirometry assessment of COPD databases collected in the department of Pulmonary Medicine at a tertiary care hospital over a period of eighteen months, following approval by the Institutional Ethics Committee (ECARP ref no-ECARP/2022/124). The study aimed to investigate the coexistence of UAO and types of UAO (e.g., variable intrathoracic or extra thoracic obstruction) in COPD patients using spirometry and flow-volume loop (FVL) analysis. Informed consent was obtained from all participants. The study included all adult cases of COPD with clinical, radiological correlation and where a spirometry report was available, or patient was able to perform spirometry test.

Patients below 18 years, diagnosed case of asthma, incomplete clinical data or diagnostic workups or not willing to participate were excluded from the study.

The spirometry was conducted using a Med graphics Profiler DX Pulmonary Diagnostic System spirometer, equipped with a dry pneumotachograph that met ATS spirometry guidelines [9]. The procedure involved inhaling to total lung capacity (TLC), followed by a forceful exhalation to residual volume (RV), and then rapid inhalation back to TLC, with a maximum of eight efforts allowed to comply with ATS standards. If a test was invalid or exceeded the limit, it was abandoned, and a new appointment was scheduled. The spirometer generated a flow-volume loop (FVL) by plotting flow on the y-axis and volume on the x-axis, with a normal FVL showing a slight cove near RV due to compressive forces during exhalation and negative pressures during inhalation. The FVLs were analyzed qualitatively for signs of UAO, such as flattening of the inspiratory or expiratory loop or box-shaped loops. These findings were reviewed by a senior pulmonology resident and confirmed by a senior professor. Additionally, two quantitative indices were used to assess UAO: Empey's index (FEV1/PEF ratio > 10 mL/L/min) and Forced Inspiratory Flow at 50% of Vital Capacity (FIF_{50} 100 L/min). The FEF_{50}/FIF_{50} ratio was also calculated to distinguish between variable extra thoracic (VET UAO) and variable intrathoracic (VIT UAO): $FEF_{50}/FIF_{50} > 1$ for VET UAO and $FEF_{50}/FIF_{50} < 0.3$ for VIT UAO. In fixed UAO the $FEF_{50}/FIF_{50}=1$. Continuous variables were reported as means with standard deviations and percentiles, while categorical variables were presented as frequencies and percentages.

The proportion of patients with UAO was determined, and statistical analysis was performed to evaluate the coexistence of UAO in COPD patients and the predictive value of FVL criteria.

Results

The study included 193 patients diagnosed with COPD with a mean age of 56.3years (±12.94), with 126 males and 67 females. Based on the etiotypes of COPD, out of 193 patients, 113 patients (58.5%) were diagnosed with COPD-I and 80 patients (41.45%) with COPD-C. All patients had breathlessness and cough. None had stridor, stertor or hoarseness of voice. Mean FEV1 was 1.25L (49.8%) and mean FVC was 1.93L(61.72). On visual assessment of FVL, 141 patients (73%) had neither inspiratory or expiratory loop flattening. FVL was abnormal in 27%

patients. Expiratory loop flattening, indicative of intrathoracic upper airway obstruction, was observed in 39 patients (20%)—including 9.3% of COPD-C and 10.8% of COPD-I patients. Inspiratory loop flattening, suggesting variable extra thoracic upper airway obstruction, was seen in 13 patients (7%)—comprising 2% of COPD-C and 5% of COPD-I patients.

FIF_{50} was less than 100 L/min in 53 patients (27.3% of the total), including 14 patients (7.25%) with COPD-C and 39 patients (20.2%) with COPD-I. None of the patients had Empey's index i.e ratio of Fev_1 to PEF > 10 mL/L/min. The FEF_{50}/FIF_{50} ratio was greater than 1 in 33 patients (17%), including 6 patients with COPD-C (3.1%) and 27 with COPD-I (13.9%), indicating variable extra thoracic obstruction. The FEF_{50}/FIF_{50} ratio was less than 0.3 in 44% of patients, including 23.8% of those with COPD-C and 20.2% with COPD-I, indicating that variable intrathoracic obstruction was the most prevalent type of upper airway obstruction. Out of a total of 193 patients, 7.21% fulfilled at least 3 out of the following 4 criteria: a) visual loop showing inspiratory or expiratory loop flattening b) $FEF_{50}/FIF_{50} < 0.3$ or $FEF_{50}/FIF_{50} > 1$,c) FIF_{50} (L/min) < 100,d) Empey's Index (FEV_1/PEF) > 10 mL/L/min. Table 1 summarizes the results of the study.

Discussion

Upper airway obstruction (UAO) is a distinct clinical condition with diverse causes, presenting acutely or chronically based on the underlying etiology and type of obstruction. It is classified as a variable UAO if obstruction changes with respiration or fixed if it remains constant. Variable UAO is further subtyped by location into variable extra thoracic (VET UAO) and variable intrathoracic (VIT UAO) [10]. In variable intrathoracic obstruction, airway narrowing varies with transmural pressure, causing reduced forced expiration but relatively normal inspiration. In contrast, variable extra thoracic obstruction impairs forced inspiration, while expiration remains largely unaffected. In fixed upper airway obstructions, the airway diameter remains unchanged despite variations in transmural pressure during inspiration and expiration. As a result, both inspiratory and expiratory airflow are reduced, regardless of whether the obstruction is intrathoracic or extra thoracic in location [11]. Patient's with UAO are usually asymptomatic unless the airway is significantly narrowed. Resting dyspnea typically occurs when the airway diameter is reduced to 5mm, while dyspnea during physical activity may appear when the diameter is around 8 mm. It's important to note that airway narrowing must be about 80% before it becomes detectable on spirometry, especially when considering factors like age, gender, and BMI. One key difference between upper airway obstruction and lower airway conditions (like obstructive or restrictive lung diseases) on spirometry is that FEV1 tends to remain nearly normal or only slightly affected in upper airway obstruction [7].

Another important tool for identifying upper airway obstruction (UAO) is Peak Inspiratory Flow (PIF), a simple, bedside, non-invasive, and quantitative parameter used to evaluate the severity of UAO. PIF is useful for assessing both the severity of obstruction and the response to treatment. It can also help detect severe obstruction early, potentially preventing emergency interventions such as tracheostomy. Limitations of PIF being it is less sensitive to mild obstruction cases. PIF may appear normal until an obstruction is severe. PIF is effort-dependent [12]. We did not use PIF in our study.

Definitive diagnosis of upper airway obstruction (UAO) involves imaging and direct visualization via laryngoscopy or bronchoscopy. However, spirometry is the most widely used pulmonary function test (PFT), which assesses both the volume and speed of airflow, making it essential for diagnosing, staging, and monitoring COPD patients and thus it is routinely done in COPD patients [10]. The flow-volume loop (FVL) can be used as screening tool for detecting the presence of upper airway obstruction (UAO) as well as identifying the site (intrathoracic or extra thoracic) and the nature (fixed or variable) of the obstruction [8,13].Therefore, both the visual appearance of the FVL envelope (Figure 1) and the calculation of upper airway indices should be considered during interpretation [8].

Until now there are several studies that have demonstrated the presence of upper airway symptoms in COPD patients Hurst et al examined a well-defined cohort of 65 patients with COPD and found that 88% of these patients reported some degree of upper airway symptoms [14]. None of the studies have been conducted for upper airway obstruction in COPD. The dynamic hyperinflation in COPD-C and parenchymal involvement in COPD-I has an impact on the upper airway and can cause UAO.

In the current study, we investigated for the co-existence of the upper airway obstruction (UAO) component in spirometry among patients with COPD.COPD present with significant airflow limitation, but the involvement of the upper airways, which may complicate the interpretation of spirometry results, has not been extensively examined. To our knowledge, our study is the first to look at this association and first to employ the upper airway obstruction criteria in patients with COPD. Our findings highlight the distinctive features of UAO in COPD patients and underscore the importance of considering upper airway involvement in their diagnostic and management strategies.

This study identified UAO components in 52 patients (27%) via flow-volume loop (FVL) analysis, with inspiratory loop flattening in 13 patients (7%) suggesting extra thoracic obstruction, predominantly in the COPD-I group. This finding aligns with literature suggesting that recurrent infections in COPD-I can lead to upper airway inflammation and edema, contributing to extra thoracic obstruction [14]. In COPD-C, Minimal inspiratory flattening likely reflects emphysema-induced lung hyperinflation, which stabilizes extra thoracic airways through tracheal traction [15]. Expiratory loop flattening (20% overall, higher in COPD-I) correlates with bronchial wall thickening and mucus plugging, consistent with infection-related small airway remodeling and expiratory airflow limitation in COPD-C likely reflects intrinsic small airway disease and emphysematous destruction, reducing elastic recoil [16,17]. Reduced FIF_{50} (<100 L/min) was observed in 27.3% of patients, predominantly in those with COPD-I (20.2% patients), suggesting upper airway narrowing due to chronic inflammation. This finding is supported by studies demonstrating elevated levels of IL-6 and TNF-α in infection-predominant COPD [18]. FEF_{50}/FIF_{50} >1 observed in 33 patients (17%) (mostly COPD-I 14%), this ratio indicates extra thoracic obstruction, consistent with laryngeal dysfunction in recurrent infection models [19]. The FEF_{50}/FIF_{50} ratio was less than 0.3 in 85 patients (44%), with COPD-C 24% and COPD-I 20% indicating that variable intrathoracic obstruction was the most prevalent type of upper airway obstruction. The high proportion of FEF_{50}/FIF_{50} <0.3 (variable intrathoracic obstruction) aligns with COPD's intrinsic small airway pathology. The absence of Empey's Index (FEV1/PEF >10) in all patients could suggest low intensity of upper airway involvement. It can also be due to selection bias, as in the original study done by Empey which included all cases with severe UAO with evident stridor on clinical examination [20]. Notably, only 7.21% met 3 diagnostic criteria for UAO (e.g., FVL flattening, FIF_{50}<100 L/min), suggesting that isolated UAO markers may lack specificity in this population [21,22].

While FVL analysis is critical for detecting UAO, its interpretation in COPD requires caution. For example, distal airway obstruction in severe COPD may mimic intrathoracic UAO on spirometry, as seen in a case where a tracheal mass was initially misdiagnosed as COPD [21]. Current guidelines stress spirometry for diagnosing obstructive lung diseases, but this study highlights the need for adjunct imaging or bronchoscopy when UAO is suspected.

Conclusions

The study found that there is an upper airway obstruction component in patients with COPD further limiting airflow and altering the flow volume loop. The added resistance from upper airway narrowing complicates spirometry, exacerbating the obstructive pattern and worsening lung function. Further research is needed to refine our understanding of how upper airway involvement impacts these diseases and to guide more effective management strategies.

Limitations

The study's retrospective design, small size and reliance on spirometry alone may under-detect structural UAO causes. Larger cohorts and longitudinal data are needed to assess UAO's impact on disease progression. Severe airflow obstruction can mask UAO on flow volume loop, requiring advanced imaging, bronchoscopy and laryngoscopy to assess its extent and correlate it with spirometry for better clinical evaluation.

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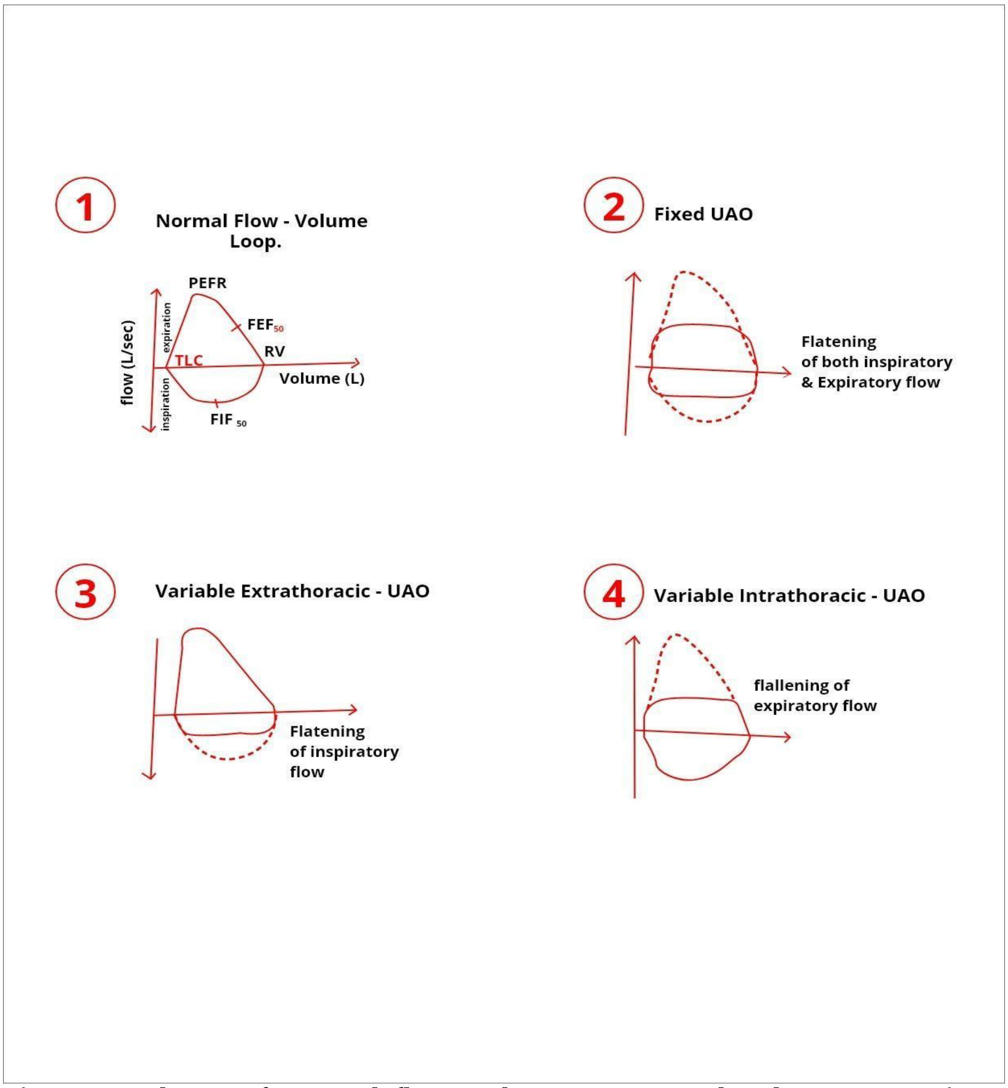

Figure 1. Shape of normal flow volume curve and volume curve in various upper airway obstructions.

Table 1. Results of qualitative and quantitative criteria for upper airway obstruction.

	UAO Criteria	Total Positive	COPD-C	COPD-I
1	**Visual FV Loop**	27%		
	Insp	13(7%)	4(2%)	9(5%)
	Exp	39(20%)	18(9%)	21(11%)
2	**FEF_{50}/ FIF_{50}**			
	<0.3	85(44%)	46(24%)	39(20%)
	>1	33(17%)	6(3%)	27(14%)
3	**FIF_{50} (L/M)**			
	<100 L/m	53(27%)	14(7%)	39(20%)
4	**Empey's Index**			
	FEV1/PEF>10 ml/L/min	0	0	0
5	**Aggregate criteria**			
	3 out of 4 criteria	14(7.2%)	3(2%)	11(6%)