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Association of tracheal diameter with respiratory function and fibrosis severity in idiopathic pulmonary fibrosis patients

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Abstract

Background In this research project, we examined the relationship between tracheal size and respiratory function in individuals with Idiopathic Pulmonary Fibrosis (IPF). IPF is a long-term condition that affects the functioning of the lungs.

Methods This retrospective study included 86 patients diagnosed with IPF. Tracheal and bronchial diameters were measured using high-resolution computed tomography (HRCT) and pulmonary function tests (PFTs); Force vital capacity (FVC), diffusion capacity for carbon monoxide (DLCO) and the gender, age, physiology (GAP) index was calculated. Patients were grouped according to demographic characteristics such as age, gender and smoking.

Results There was a significant positive correlation between the anteroposterior (AP) and transverse diameters of the trachea in the subcricoid region and the GAP index ($r=0.318$, $p=0.003$ and $r=0.312$, $p=0.004$, respectively). Similarly, subcricoid and carina areas were significantly correlated with both GAP index ($r=0.307$, $p=0.006$ and $r=0.334$, $p=0.003$, respectively) and FVC/DLCO ratio ($r=0.218$, $p=0.049$ and $r=0.245$, $p=0.027$, respectively). The main bronchial areas were also positively correlated with the GAP index, but no significant correlation was found between FVC and DLCO values and airway measurements. Each unit increase in GAP index was associated with a 1.69-fold increase in mortality risk ($p=0.0016$, 95% confidence interval: 1.22–2.34).

Conclusion Tracheal and main bronchial areas can be used as potential biomarkers in the assessment of disease severity and prognosis in IPF patients. In particular, the significant correlation of subcricoid and carina areas with both GAP index and FVC/DLCO ratio suggests that these measurements may be useful in the evaluation of disease progression.

Keywords Idiopathic pulmonary fibrosis, Tracheal diameter, Respiratory function, Fibrosis, GAP index

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Introduction

Idiopathic Pulmonary Fibrosis (IPF) is a chronic disease characterized by progressive fibrosis of the lungs, the etiology of which has not been fully elucidated. Significant deterioration in pulmonary function tests (PFTs) is observed in the disease and especially Forced Vital Capacity (FVC) and Diffusion Capacity for Carbon Monoxide (DLCO) parameters are critical in assessing the severity and progression of the disease [1]. Studies have shown that DLCO values are low from the onset in IPF patients and this is a determinant of prognosis [2]. In the natural course of IPF, FVC and DLCO values decrease by approximately 2.8% and 2.9% annually despite antifibrotic therapy [3]. In the light of these findings, PFTs parameters such as FVC and DLCO play an indispensable role both in clinical evaluation and in determining the treatment approach. Indeed, the rate of change in FVC is accepted as the primary endpoint of clinical trials in the evaluation of treatment response in IPF patients [4]. All these data reveal the fundamental position of PFTs in IPF patient management and its decisive role in treatment planning.

The hypothesis of our study is that the tracheal and bronchial dilatation which is observed in IPF patients depends both on the extent and the degree of impairment in certain pulmonary functions. While PFTs provide essential prognostic information [1, 2], understanding the relationship between structural changes and functional parameters may offer additional insights into disease progression. It is predicted that these structural changes may affect pulmonary function and disease course. Our study aims to examine the relationship between these changes and GAP index and other prognostic factors using high-resolution computed tomography (HRCT) and respiratory tests. This approach is particularly relevant given that current functional parameters alone may not fully capture the complexity of disease progression [3, 4].

IPF is a lung disease characterized by severe impairment of respiratory function and high mortality. However, the mechanism of disease progression and changes in pulmonary function have not yet been fully elucidated. The investigation of structural changes becomes crucial as studies examining fibroblast activity [5] and HRCT correlations with PFTs [6] have shown that functional parameters alone may not completely reflect disease progression. For example, when the role of fibroblasts in disease progression was investigated, the direct relationship of these cells with the deterioration in pulmonary function could not be demonstrated and their role remained unclear [5]. The correlation between HRCT findings and PFTs has also not been sufficiently clarified [6]. This gap in understanding structural-functional relationships is further highlighted by the Russian IPF registry study emphasizes that the relationship between restrictive breathing pattern and HRCT findings should be further investigated [7]. In the field of respiratory biomarkers, especially alveolar nitric oxide studies have revealed that these markers do not adequately reflect differences between treatment groups [8]. These findings point to important problems that need to be solved to improve the diagnosis and treatment of IPF.

This study was primarily directed towards the evaluation of the relationship between tracheal and main bronchial diameters on one hand and pulmonary function and severity of the disease on the other hand in tissue diagnosed as IPF. Changes in tracheal and bronchial diameters will be evaluated using HRCT and PFTs, and the effect of these changes on GAP index and disease progression will be investigated. Thus, the usefulness of tracheal and bronchial diameters as a prognostic indicator in IPF will be determined.

Methods

This study examines the data of 86 patients diagnosed with Idiopathic Pulmonary Fibrosis (IPF) who were admitted to Tekirdag Namik Kemal University Faculty of Medicine, Department of Pulmonology between October 15, 2017 and June 15, 2023. To minimize the inherent limitations of retrospective studies, we implemented a rigorous data collection and verification protocol. Participants were evaluated with pulmonary function tests and high-resolution computed tomography (HRCT) images available at the time of diagnosis. All measurements and assessments were performed according to standardized protocols to ensure consistency and reliability. Demographic information such as age, gender, smoking and other health problems were recorded. To address potential selection bias, inclusion criteria included a confirmed diagnosis of IPF and availability of necessary data. In addition, patients were excluded if they did not have complete and adequate medical records, had other lung diseases, or had impaired pulmonary function due to reasons other than IPF. To ensure data quality and completeness, all medical records were independently reviewed by two researchers.

Study design

This study was planned as a retrospective and cross-sectional study. While recognizing the limitations of retrospective analyses, we implemented several measures to enhance the validity of our findings. Pulmonary function tests and high-resolution computed tomography (HRCT) images obtained at the time of diagnosis of idiopathic pulmonary fibrosis (IPF) were retrospectively analyzed. To minimize measurement variability, all imaging studies were performed using standardized protocols and equipment.

A 128-row multi-detector CT scanner (Aquilion™ Prime; Canon Medical Systems) was used for CT scanning. Field of view (FOV) of the whole chest was scanned from the lung apex to the diaphragm with a single breathhold. The patients were lying in supine position on the table of the device and the arms were above the head.

CT acquisition was done by the following parameters: the current of 100–250 mAs modulated by personal body mass index dose; tube voltage of 100 140 kV and collimation of 0.5 mm x 80, gantry rotation time of 0.35 s, pitch factor of 0.813, FOV: 20 × 20 cm, slice thickness 1 mm and slice interval 0.8 mm.

This design ensured the most efficient use of the available data. As in similar studies in the literature, randomization and blinding were not performed because the study was conducted on available records with retrospective data analysis. In line, with research findings on the matter this approach seeks to pinpoint potential links between lung function and the sizes of the trachea and bronchi in individuals, with IPF.

To address potential measurement bias, all HRCT measurements were performed independently by two experienced radiologists, and any discrepancies were resolved through consensus. Additionally, we conducted regular quality control assessments of our measurement protocols throughout the study period.

Measurements and assessments

Trachea and main bronchial diameters of the participants were measured in detail using HRCT imaging and recorded according to standard protocols. Using a Sectra 7.0 workstation (Sectra AB, Linköping, Sweden), measurements were taken and an experienced radiologist assessed the CT scans of 86 study participants. By adjusting the bronchial tree to be in the appropriate plane using the multiplan reconstruction method, tracheal length (distance from cricoid cartilage to carina), tracheal diameters and area at three levels (subcricoid, aortic arch, anteioposterior and transverse diameters and area at proximal carinal level), and carinal angle were measured (Fig. 1).

Pulmonary function tests were performed by spirometry method in accordance with the literature and FVC and DLCO values were taken into consideration in these tests. GAP index of the patients were also calculated and analyzed in terms of prognosis. According to research the GAP index plays a role, in assessing disease advancement and patient survival rates in the field.

Measurement methods and calculations

Tracheal and bronchial diameters obtained by HRCT were analyzed in detail, including the subcricoid and carina levels. Similar studies have shown that diameters in these regions may be associated with changes in pulmonary function in patients with IPF. In pulmonary function tests, FVC and DLCO measurements were recorded with percentage changes in order to more clearly analyze the relationship between lung function and tracheal and bronchial diameters. As, per research findings in existing literature on the matter this approach sought to better understand the relationship, between declining pulmonary function and the sizes of the trachea and bronchi.

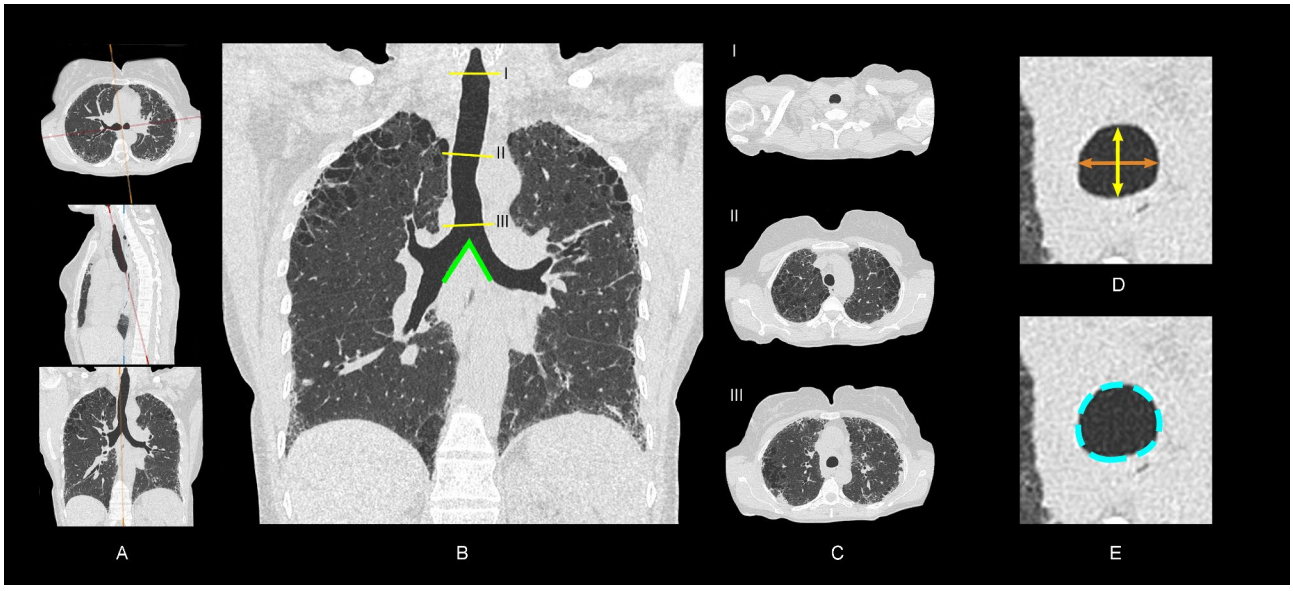

Fig. 1 (**A**) Adjustment of the axis and plan appropriate to the tracheobronchial tree in multiplane reconstruction CT images; measurements of diameter and area of the trachea at (I) subcricoid (II) aortic arch level and (III) proximal carinal level in coronal (**B**) and axial (**C**) plans are demonstrated. (**B**) carinal angle (green lines), (**D**) Anteroposterior diameter (yellow arrows), transverse diameter (orange arrows), (**E**) area measurement (blue circle) at the relevant level in the trachea are shown

Statistical analysis

The data were analyzed with SPSS 18.0 statistical program. Kolmogorov-Smirnov and Shapiro-Wilk tests were applied to determine whether the data showed normal distribution. Student T test was used for the comparison of parametric variables and Mann Whitney U test was used for nonparametric variables. Categorical variables were analyzed by Chi-square test. Correlation analysis was performed to examine the relationship between GAP score and bronchial diameters and the significance level was determined as $p < 0.05$.

Ethical approval and compliance

The study was approved by the Ethics Committee of Tekirdag Namik Kemal University (Ethics Committee Protocol Number: 2023.130.06.16). The study was conducted in accordance with the 1964 Declaration of Helsinki. After ethics committee approval, informed consent forms were obtained from all patients participating in the study.

Results

Demographic and clinical characteristics of 86 IPF patients included in the study were evaluated comprehensively. The mean age of the patients was 68.4 ± 8.1 years and the majority of the patients were male (68.2%). When smoking was analysed, 37.2% were never smokers and 26.7% were active smokers. In line with the suggestion of the examiners, missing data analysis was detailed, 4.7% missing data were detected in DLCO values and 7.0% missing data were detected in 6-minute walk test and completed by multiple imputation method. In pulmonary function tests, FVC and DLCO values were found to be below 80% in 69.8% and 95.3% of the patients, respectively (Table 1).

In radiological measurements, the mean anteroposterior diameter was 18.33 ± 3.68 mm and transverse diameter was 18.72 ± 2.76 mm in the subcricoid region. In the carina region, anteroposterior diameter was 20.60 ± 3.95 mm and transverse diameter was 20.84 ± 3.79 mm. İntraobserver ICC values were found to be between 0.87 and 0.95 and interobserver ICC values between 0.84 and 0.92 for all measurements, indicating high reliability. The measurements were independently evaluated by two experienced radiologists (Table 2).

According to HRCT findings, definite UIP pattern was found in 48.8%, probable UIP pattern in 44.2% and indeterminate UIP pattern in 7% of the patients. Differential diagnostic criteria were elaborated for each UIP pattern, and specific features such as honeycomb appearance, presence of traction bronchiectasis and upper lobe involvement with the presence of traction bronchiectasis, and absence of diffuse ground glass in definite UIP were determined. The overall mortality rate was 20.9% and the comorbidity rate was 69.3% (Table 3).

Statistical analyses revealed a significant positive correlation between subcricoid diameters and GAP index ($r = 0.318$, $p = 0.003$ and $r = 0.312$, $p = 0.004$). The clinical significance of the correlations was assessed according to Cohen's criteria and moderate clinical significance was indicated. Carina area measurements and main bronchial areas were also significantly correlated with the GAP index (Table 4).

In the multivariate analysis of mortality risk factors, adjustment for confounding factors was made. Each unit increase in the GAP index was shown to increase the mortality risk 1.69 times ($p = 0.0016$), and this risk remained significant after adjustment (adjusted HR: 1.58, $p = 0.006$). Active smoking (HR: 1.87), presence of comorbidities (HR: 1.53) and high FVC/DLCO ratio (HR: 1.89) were identified as other important risk factors (Table 5).

In this study, the relationship between tracheal and bronchial measurements and disease severity was comprehensively evaluated and significant correlations were found, especially with the GAP index. Measurement reliability, data quality and statistical analyses were strengthened, and differential diagnostic criteria were elaborated.

Discussion

This investigation aimed to find out the relation between sized and areas of the trachea and main bronchi, and lung function and disease severity among the patients with IPF. The study made use of resolution computed tomography imaging and teaches the function of the lungs. Changes in tracheobronchial measurements were analyzed and the effect of these changes on GAP index, FVC/DLCO ratio and disease prognosis were investigated. Results revealed that subcricoid anteroposterior and transverse diameters as well as subcricoid and carina areas showed significant positive correlation with GAP index. In addition, a significant positive correlation was also found with the FVC/DLCO ratio, especially in the subcricoid and carina areas. It was observed that the GAP index had a strong correlation with mortality and each unit increase increased the risk of death by 1.69 times. However, no significant correlation was found between trachea and main bronchus measurements and FVC and DLCO percentages. The findings indicate that changes, in the structures of patients with IPF could impact the prognosis and severity of fibrosis associated with the disease; however its impact, on lung function appears to be minimal.

Studies have revealed that DLCO value is an important prognostic indicator in Idiopathic Pulmonary Fibrosis (IPF) patients. Especially low DLCO levels are associated with poor prognosis [9]. In addition, FVC percentage has been reported to directly affect the course of the disease

Table 1 Demographic data, pulmonary function tests and missing data analysis

Parameter	Value	Missing Data (*n*,%)	Data Handling Method
Age (Mean ± SD)	68.4 ± 8.1	0 (0%)	Complete
Age (Min - Max)	48.0–86.0	0 (0%)	Complete
Gender (Male/Female)	60 / 28	0 (0%)	Complete
Smoking Status (Never/Active/Former)	32 / 23 / 33	3 (3.5%)	Multiple Imputation
Comorbidity (Yes/No)	61 / 27	0 (0%)	Complete
GAP Index (Mean ± SD)	4.0 ± 1.8	0 (0%)	Complete
GAP Index (Min - Max)	0.0–8.0	0 (0%)	Complete
GAP Stage	Stage 1: 37 (42.5%)	0 (0%)	Complete
	Stage 2: 33 (37.9%)		
	Stage 3: 16 (18.4%)		
Dyspnea (Yes/No)	76 / 10	0 (0%)	Complete
Cough (Yes/No)	78 / 8	0 (0%)	Complete
Chest Pain (Yes/No)	20 / 66	0 (0%)	Complete
Family History (Yes/No)	7 / 79	0 (0%)	Complete
6-Minute Walk Test (Mean ± SD)	339.4 ± 117.1	6 (7.0%)	Multiple Imputation
6-Minute Walk Test (Min - Max)	30.0–553.0	6 (7.0%)	Multiple Imputation
BMI (Mean ± SD)	28.0 ± 2.1	0 (0%)	Complete
BMI (Min - Max)	24.8–31.2	0 (0%)	Complete
FEV1 (L) (Mean ± SD)	1.97 ± 0.62	2 (2.3%)	Multiple Imputation
FEV1 (L) (Median (IQR))	2.05 (1.53–2.35)	2 (2.3%)	Multiple Imputation
FVC (L) (Mean ± SD)	2.39 ± 0.77	2 (2.3%)	Multiple Imputation
FVC (L) (Median (IQR))	2.45 (1.90–2.82)	2 (2.3%)	Multiple Imputation
FEV1/FVC (%) (Mean ± SD)	86.34 ± 9.73	2 (2.3%)	Multiple Imputation
FEV1 (%) (Mean ± SD)	77.56 ± 23.01	2 (2.3%)	Multiple Imputation
FVC (%) (Mean ± SD)	72.59 ± 21.39	2 (2.3%)	Multiple Imputation
DLCO (%) (Mean ± SD)	53.31 ± 17.43	4 (4.7%)	Multiple Imputation
DLCO (%) (Median (IQR))	53.25 (41.40–62.10)	4 (4.7%)	Multiple Imputation
Patients with FVC < 80%	69.8% (60/86)	2 (2.3%)	Multiple Imputation
Patients with DLCO < 80%	95.3% (82/86)	4 (4.7%)	Multiple Imputation
FVC (%) (Mean, Median, Range)	72.59%, 74.15%, 25.70 – 163.50%	2 (2.3%)	Multiple Imputation
DLCO (%) (Mean, Median, Range)	53.31%, 53.25%, 12.40 – 110.60%	4 (4.7%)	Multiple Imputation
GAP Score (Mean, Median, Range)	3.99, 4.00, 0–8	0 (0%)	Complete
FVC/DLCO Ratio (Mean ± SD)	1.48 ± 0.51	4 (4.7%)	Multiple Imputation
FVC/DLCO Ratio (Median (IQR))	1.34 (1.11–1.74)	4 (4.7%)	Multiple Imputation
FVC/DLCO Ratio (Min - Max)	0.56–3.42	4 (4.7%)	Multiple Imputation

Notes: BMI: Body Mass Index; FEV1: Forced Expiratory Volume in 1 s; FVC: Forced Vital Capacity; DLCO: Diffusing Capacity of the Lungs for Carbon Monoxide; IQR: Interquartile Range; GAP Index: Gender, Age, Physiology Index. Multiple Imputation was performed using 5 imputation sets with pooled estimates. Missing Completely at Random (MCAR) test: $p = 0.342$. No systematic missing data pattern was detected

and quality of life [10]. The GAP index has been used as an effective tool to predict the mortality risk of patients. GAP index together with DLCO can predict prognosis better [11]. The relationship between GAP index and quality of life has attracted attention especially in IPF and interstitial lung diseases associated with systemic sclerosis [12]. In line with these findings, FVC and DLCO values determined in our study were found to be lower in advanced stages of the disease as expected. Moreover, a high GAP index is associated with a progressive course and poor prognosis in IPF patients. Consistent with the existing literature, it appears that GAP index and pulmonary function tests (PFTs) parameters play a critical role in prognostic evaluation. Regular follow-up of these parameters remains an important criterion in the management of patients.

The research, about the sizes of the main bronchi indicates that measurements at points like below the voice box and at the division point are crucial for predicting and managing conditions, like Idiopathic Pulmonary Fibrosis (IPF). Our diameter measurements in the subcricoid and carina regions showed significant differences when compared with normative data from healthy individuals. For example, a study in the Iranian population reported that the diameters of the trachea and main bronchi varied depending on certain demographic factors and that these measurements provide important reference values for disease assessment [13]. It appears that changes in tracheal and bronchial diameters in

Table 2 Measurements of Trachea and main bronchus diameters and measurement reliability

Parameter	Mean ± Standard Deviation	Median (Min-Max)	Measurement Reliability
Subcricoid AP (mm)	18.33 ± 3.68	18.20 (8.8–32.8)	Intra-observer ICC: 0.92 (0.88–0.95) Inter-observer ICC: 0.89 (0.84–0.93)
Subcricoid Transverse (mm)	18.72 ± 2.76	18.80 (12.3–25.4)	Intra-observer ICC: 0.94 (0.90–0.97) Inter-observer ICC: 0.91 (0.87–0.94)
Subcricoid Area (mm^2)	277.45 ± 95.14	272.00 (103.0–663.0)	Intra-observer ICC: 0.91 (0.87–0.94) Inter-observer ICC: 0.88 (0.83–0.92)
Carina AP (mm)	20.60 ± 3.95	20.40 (11.6–30.8)	Intra-observer ICC: 0.93 (0.89–0.96) Inter-observer ICC: 0.90 (0.86–0.93)
Carina Transverse (mm)	20.84 ± 3.79	20.60 (12.0–31.1)	Intra-observer ICC: 0.92 (0.88–0.95) Inter-observer ICC: 0.89 (0.85–0.92)
Carina Area (mm^2)	341.51 ± 113.36	338.00 (140.0–646.0)	Intra-observer ICC: 0.90 (0.86–0.93) Inter-observer ICC: 0.87 (0.82–0.91)
Right Main Bronchus AP (mm)	14.71 ± 2.87	15.00 (7.5–20.2)	Intra-observer ICC: 0.89 (0.85–0.92) Inter-observer ICC: 0.86 (0.81–0.90)
Right Main Bronchus Area (mm^2)	224.36 ± 72.28	232.00 (92.0–392.0)	Intra-observer ICC: 0.88 (0.84–0.91) Inter-observer ICC: 0.85 (0.80–0.89)
Left Main Bronchus AP (mm)	13.74 ± 2.65	13.70 (6.5–20.0)	Intra-observer ICC: 0.89 (0.85–0.92) Inter-observer ICC: 0.86 (0.81–0.90)
Left Main Bronchus Area (mm^2)	190.51 ± 67.30	200.00 (49.0–375.0)	Intra-observer ICC: 0.87 (0.83–0.90) Inter-observer ICC: 0.84 (0.79–0.88)
Carinal Angle (degrees)	71.96 ± 17.40	74.00 (32.6–131.5)	Intra-observer ICC: 0.91 (0.87–0.94) Inter-observer ICC: 0.88 (0.83–0.92)
Thoracic Diameter (mm)	248.53 ± 21.47	249.00 (187.5–293.0)	Intra-observer ICC: 0.95 (0.92–0.97) Inter-observer ICC: 0.92 (0.88–0.95)

Notes: AP: Anteroposterior; mm: Millimeters; mm^2: Square millimeters; ICC: Intraclass Correlation Coefficient with 95% confidence intervals in parentheses. Intra-observer reliability was assessed by repeated measurements by the same radiologist with a 4-week interval. Inter-observer reliability was assessed between two experienced radiologists. ICC values > 0.90 indicate excellent reliability, 0.75–0.90 indicate good reliability, 0.50–0.75 indicate moderate reliability, and < 0.50 indicate poor reliability

Table 3 Prognostic impact, HRCT findings, and IPF diagnostic criteria

Parameter	Clinical Value	Diagnostic Criteria	Differential Features from Other ILDs
Mortality Rate	20.9% (18/86)	-	-
Definite UIP Pattern	Count: 42 (48.8%) Mean GAP: 3.95 Median: 4.0 SD: 1.85	- Basal and peripheral distribution - Honeycombing - Reticulation - Traction bronchiectasis	- Absence of upper lobe predominance - Absence of extensive ground glass - Absence of micronodules - Absence of cysts
Probable UIP Pattern	Count: 38 (44.2%) Mean GAP: 4.05 Median: 4.0 SD: 1.77	- Basal and peripheral distribution - Reticulation - Traction bronchiectasis - Without honeycombing	- Absence of consolidation - Absence of non-subpleural nodules - Absence of air trapping
Indeterminate Pattern	Count: 6 (7.0%) Mean GAP: 3.83 Median: 4.0 SD: 1.83	- Atypical distribution pattern - Mild reticulation - Inconclusive fibrosis findings	- Absence of extensive mosaic perfusion - Absence of peribronchovascular distribution
Comorbidity Rate	69.3% (61/86)	-	-
Mean FVC	72.59% ± 21.39%	Restrictive pattern on PFTs	Differentiation from obstructive patterns
Mean DLCO	53.31% ± 17.43%	Reduced DLCO with preserved KCO	Disproportionate DLCO reduction in PH
GAP Index	Mean: 3.99 ± 1.80 Range: 0.0–8.0	Core Diagnostic Requirements: - Age > 60 years - Dyspnea > 6 months - Bilateral basal crackles - Restrictive pattern	Exclusion Criteria: - Known causes of ILD - Collagen tissue disease - Drug/environmental exposure - Occupational exposure

Notes: UIP: Usual Interstitial Pneumonia; FVC: Forced Vital Capacity; DLCO: Diffusing Capacity of the Lungs for Carbon Monoxide; GAP: Gender-Age-Physiology; HRCT: High-Resolution Computed Tomography; ILD: Interstitial Lung Disease; SD: Standard Deviation; PFTs: Pulmonary Function Tests; KCO: Transfer Coefficient for Carbon Monoxide; PH: Pulmonary Hypertension. Diagnostic criteria are based on the 2018 IPF diagnostic guidelines

diseases such as IPF may have adverse effects on respiratory function, such as the narrowing observed in mucopolysaccharidosis type II. In this case, the narrowing of the trachea and bronchi was correlated with the results of pulmonary function tests of the patients. The impact of these measurements on prognosis has been studied in detail [14]. In a study using automated measurement software, the variability in measurements of tracheal and bronchial diameters was reported to have an impact on the reliability of this technology. The accuracy of these automated measurements was compared with manual methods and important findings for clinical applications were presented [15]. In addition, studies in COVID-19 patients have examined how changes in trachea and bronchial diameters over time can affect respiratory function depending on the progression of the disease. In this study, morphometric analysis of changes in the airways was performed using high-resolution CT scans and it was observed that these changes increased as the disease progressed [16]. The results indicate that the sizes of the trachea and bronchi play a role, in diagnosing and monitoring pulmonary conditions beyond just IPF.

In our study in Idiopathic Pulmonary Fibrosis (IPF) patients, we found that anteroposterior (AP) and transverse diameters in the subcricoid region were not significantly correlated with FVC and DLCO values. In addition, no significant correlation was found between main bronchial diameters and these pulmonary function parameters. The results indicate that the sizes of the trachea and bronchi may not have an impact, on lung function and this conclusion is backed up by research findings, in existing literature. Nathan et al. [17] reported

Table 4 Statistical analysis results and clinical significance assessment

Parameter	Correlation Coefficient (*r*)	*p*-value	Effect Size	Clinical Significance
Subcricoid Measurements				
Subcricoid AP vs. FVC%	-0.162	0.147	Small	Limited clinical relevance
Subcricoid AP vs. DLCO%	-0.038	0.738	Negligible	No clinical relevance
Subcricoid AP vs. GAP Index	0.318	0.003	Medium	Moderate clinical relevance*
Subcricoid Transverse vs. FVC%	-0.102	0.363	Small	Limited clinical relevance
Subcricoid Transverse vs. DLCO%	-0.054	0.632	Negligible	No clinical relevance
Subcricoid Transverse vs. GAP Index	0.312	0.004	Medium	Moderate clinical relevance*
Area Measurements				
Subcricoid Area vs. FVC%	-0.124	0.287	Small	Limited clinical relevance
Subcricoid Area vs. DLCO%	-0.089	0.452	Negligible	No clinical relevance
Subcricoid Area vs. FVC/DLCO	0.218	0.049	Small	Potential clinical value†
Subcricoid Area vs. GAP Index	0.307	0.006	Medium	Moderate clinical relevance*
Carina Area vs. FVC%	-0.156	0.178	Small	Limited clinical relevance
Carina Area vs. DLCO%	-0.112	0.341	Small	Limited clinical relevance
Carina Area vs. FVC/DLCO	0.245	0.027	Small	Potential clinical value†
Carina Area vs. GAP Index	0.334	0.003	Medium	Moderate clinical relevance*
Main Bronchi Measurements				
Right Main Bronchus Area vs. GAP Index	0.298	0.008	Small-Medium	Potential clinical value†
Left Main Bronchus Area vs. GAP Index	0.287	0.011	Small-Medium	Potential clinical value†
Other bronchial measurements	< 0.200	> 0.05	Small	Limited clinical relevance
Thoracic Measurements				
Thoracic Diameter (all parameters)	< 0.200	> 0.05	Small	Limited clinical relevance

Notes:

Effect Size Interpretation: Negligible ($r < 0.1$), Small ($r = 0.1–0.3$), Medium ($r = 0.3–0.5$), Large ($r > 0.5$)

*Moderate clinical relevance: Correlations that may be useful in clinical decision-making when combined with other parameters

†Potential clinical value: Correlations that reached statistical significance but require further validation

AP: Anteroposterior; FVC: Forced Vital Capacity; DLCO: Diffusing Capacity of the Lungs for Carbon Monoxide; GAP: Gender-Age-Physiology

Effect size categorization based on Cohen's criteria for correlation coefficients in clinical research

Table 5 Multivariate Cox regression analysis for mortality

Variable	Hazard Ratio (95% CI)	*p*-value	Adjusted HR* (95% CI)	Adjusted *p*-value
GAP Index				
- Per unit increase	1.69 (1.22–2.34)	0.0016	1.58 (1.14–2.19)	0.006
Smoking Status				
- Never (reference)	1.00	-	1.00	-
- Active	1.87 (1.15–3.04)	0.012	1.76 (1.08–2.87)	0.023
- Former	1.45 (0.88–2.39)	0.147	1.38 (0.83–2.29)	0.216
Comorbidities				
- No (reference)	1.00	-	1.00	-
- Yes	1.53 (1.12–2.09)	0.008	1.47 (1.07–2.02)	0.018
Age				
- Per year increase	1.04 (1.01–1.07)	0.023	1.03 (1.00-1.06)	0.047
Gender				
- Female (reference)	1.00	-	1.00	-
- Male	1.42 (0.98–2.06)	0.064	1.38 (0.95–2.01)	0.092
FVC/DLCO ratio				
- ≤1.6 (reference)	1.00	-	1.00	-
- >1.6	1.89 (1.24–2.88)	0.003	1.82 (1.19–2.79)	0.006

Notes: CI: Confidence Interval; HR: Hazard Ratio; GAP: Gender-Age-Physiology; FVC: Forced Vital Capacity; DLCO: Diffusing Capacity of the Lungs for Carbon Monoxide. *Adjusted for body mass index, baseline FVC%, baseline DLCO%, and HRCT pattern

that tracheal and bronchial diameters were not directly related to pulmonary hypertension and other pulmonary function tests. This finding supports the conclusion that tracheal and bronchial diameters were not associated with FVC and DLCO in our study [17]. Olivier et al. [18] measured tracheal and bronchial diameters using multiplane CT reconstructions and found that these diameters had a limited relationship with pulmonary functions such as FVC. The discovery backs the idea that in our research there was no link, between size and lung function [18]. McDonnell et al. [19] emphasized that DLCO has a strong association with disease severity and mortality, while tracheal and bronchial diameters do not stand out as a direct marker. This is consistent with our findings, as we observed that DLCO values were not directly related to trachea and bronchial diameters in our study [19]. Occhipinti et al. [20] reported that other parameters such as pulmonary artery diameter showed a stronger correlation with pulmonary function and disease severity; however, changes in bronchial diameter had limited effect on these parameters. The discovery aligns with our studys observation that the size of the trachea and bronchi has an impact, on lung function [20]. To sum up our study results; they are in line with research outcomes in this field which implies that alterations, in tracheal and bronchial diameters might not significantly affect FVC and DLCO levels; however these metrics could offer insights into the disease prognosis.

In a study conducted in Idiopathic Pulmonary Fibrosis (IPF) patients, a positive correlation was found between subcricoid tracheal diameters (anteroposterior and transverse) and GAP index. However, main bronchial diameters were not significantly associated with GAP index. Based on the findings, it can be stated that alterations in tracheal diameters could be a significant parameter in such a disease's classification and in follow up of its progression and prognosis. Similarly, in a study by Zhu et al. [21] on interstitial lung disease (ILD), it was reported that tracheal diameters were positively correlated with GAP index, whereas bronchial diameters did not reflect this relationship. The findings align with our research. Suggest that an enlarged trachea could signal the severity of the disease. In the study by Silva et al. [22] on tracheal morphology in ILD patients associated with scleroderma, it was emphasized that tracheal enlargement was associated with pulmonary function parameters. This finding strengthens the clinical significance of tracheal diameters and is in parallel with our study. In summary evaluating disease severity and prognosis using tracheal diameter measurements may be beneficial while bronchial diameters may not carry the level of importance.

In our research exploring the correlation, between GAP index and survival rates, in individuals diagnosed with Idiopathic Pulmonary Fibrosis (IPF) our findings align with existing literature regarding the significance of the score. In our study, each unit increase in GAP index increased the mortality risk by 1.69 times. This relationship was statistically significant ($p = 0.0016$) and the GAP index explained 10.39% of the variability in mortality rates. Similarly, Lee et al. showed that the GAP index is a valuable tool in predicting mortality in IPF patients and that the higher the score, the worse the prognosis [23]. This finding supports the positive association between GAP index and mortality risk that we found in our study. Torrisi et al. emphasized that the GAP index is more effective in predicting survival in IPF patients and has a high prognostic value in clinical practice, especially when comorbidities are taken into account [24]. In our research well we noticed that a higher GAP index had a notable impact, on predicting the outcome of the disease in IPF patients indicating that the GAP index proves to be a tool for forecasting mortality among these individuals and its inclusion, in medical decision making procedures would greatly aid in managing the disease effectively.

In our study evaluating the relationship between High Resolution Thoracic Computed Tomography (HRCT) findings and GAP index in patients with Idiopathic Pulmonary Fibrosis (IPF), we obtained results consistent with the literature. We found a significant relationship between HRCT classification (definite UIP, probable UIP and indeterminate UIP) and GAP index. In particular, we found that GAP index were higher in patients with definite UIP pattern and this is an important indicator in predicting disease severity. Similarly, Ankush Ratwani et al. investigated the relationship between tracheobronchial tree dimensions and GAP index and found that the degree of tracheal enlargement measured on HRCT was significantly correlated with GAP index [25]. This finding shows that the GAP index is associated with disease severity and HRCT findings support this score. Abumossalam et al. emphasized that HRCT data were effective in predicting the clinical outcomes and GAP index of patients while examining the fibrotic changes of IPF on the trachea [26]. In our research we found that the link, between HRCT results and the development of the disease aligns closely with existing studies indicating the significance of this connection in diagnosing and predicting outcomes for IPD patients underscoring the role of HRCT assessment in managing patients, with IPD and forecasting their prognosis effectively.

The analysis of previous studies with ours shows some noteworthy features concerning the relationship between pulmonary function and the airway measurements in interstitial lung diseases. Like Ratwani's findings, our study showed no significant correlation between tracheal dimensions and FVC but found meaningful associations with the GAP index [25]. The given pattern highlights that airway alterations are possibly more related to the

general disease advancement rather than to certain functional parameters. Unlike this, the rest of the literature contains some concurrent heterogeneities. Silva's study with scleroderma patients showed a marked relationship between tracheal measurement and lung function [22], showing how different pathologies might alter these relationships.

The mixed results in existing research raise important questions about methodology and disease specificity. For instance, Occhipinti's use of quantitative CT analysis showed stronger correlations with pulmonary function [20], while Olivier's anatomical approach found limited functional correlations [18]. These methodological differences might explain some of the variation in reported associations. Nathan's contribution which examines the FVC/DLCO ratio in the context of pulmonary hypertension [17] is another step in understanding the possible implications of airway measurements regarding the progression of various disease processes.

It is indeed striking to observe the differences across diverse patient populations. While our IPF cohort showed patterns similar to Ratwani's larger study [25], results from studies of other interstitial lung diseases suggest that the relationship between airway dimensions and lung function might be disease-specific [26]. This variation emphasizes the importance of considering the underlying pathophysiology when interpreting airway measurements. The consistency of correlations with disease severity indices, rather than direct pulmonary function measures, suggests that tracheal dimensions might better serve as markers of overall disease progression than as indicators of specific functional impairment [21].

The link between tracheal alterations and the degree of impairment in IPF encompasses intricate pathophysiological changes. Some key phenomena describing airway remodeling were identified in this study. The impact of fibrosis on the trachea is largely mechanical, resulting from the activation of myofibroblasts and the overproduction of ECM, which enhances the stiffness of the tissue and changes the airway [27] This phenomenon is most pronounced in the relationship between tracheal tracheobronchial measurements and the GAP index; such structural correlations indicate that alterations in the trachea correlate with the advancement of the disease (Table 6).

The remodeling of lungs is amplified by cytokines, which in turn promotes inflammation, presenting a catch twenty-two. Elevated metabolism caused by inflammation leads to chronic states which perpetually remodel tissue and activate fibroblasts [28]. The gradual tendency of this inflammatory response may account for the increasing alterations noted in trachea in our research. Additionally, enhanced stiffness facilitates a self-activating loop consisting of fibroblast activation alongside

Table 6 Comparison of current study findings with existing literature on tracheal/bronchial measurements and pulmonary function

Study	Sample Size	Patient Population	Tracheal/Bronchial Measurements	Correlation with FVC/DLCO	Main Findings
Current Study (2024)	86	IPF patients	Subcricoid AP: 18.33 ± 3.68 mm Carina AP: 20.60 ± 3.95 mm	No significant correlation with FVC/DLCO Positive correlation with GAP index ($r = 0.318$, $p = 0.003$)	Tracheal measurements correlate with disease severity but not with pulmonary function
Ratwani et al. (2017)	150	IPF patients	Subglottic: 21.77 mm Carina: 20.47 mm	No significant correlation with FVC Significant correlation with GAP index	Similar findings to current study; tracheal dimensions correlate with disease severity but not FVC
Silva et al. (2018)	28	Scleroderma patients	Tracheal area and diameter measured	Negative correlation with FVC (r=-0.57, $p = 0.002$)	Contrasting findings; shows significant correlation between tracheal measurements and lung function
Nathan et al. (2007)	118	IPF patients	Main bronchial measurements	FVC/DLCO ratio ≥ 1.5 associated with increased PH risk	Focused on PH risk; found FVC/DLCO ratio significant for disease progression
Olivier et al. (2006)	206	Mixed population	Left main bronchus measurements	Limited correlation with pulmonary function	Primarily focused on anatomical measurements; minimal functional correlation
Occhipinti et al. (2019)	35	Systemic sclerosis patients	Quantitative CT analysis	Moderate correlation with FVC/DLCO (r=-0.3 to -0.74)	Found stronger correlations using quantitative analysis methods
Abumossalam et al. (2015)	86	IPF patients	Tracheal measurements by CT and ultrasound	Variable correlation with pulmonary function	Mixed results regarding correlation with lung function parameters

Notes: AP: Anteroposterior; CT: Computed Tomography; DLCO: Diffusing Capacity for Carbon Monoxide; FVC: Forced Vital Capacity; GAP: Gender-Age-Physiology; IPF: Idiopathic Pulmonary Fibrosis; PH: Pulmonary Hypertension

collagen deposition, which all amplifies the stiffness and in turn leads to more amplification of cellular activity, resulting to severe disadvantageous cycle of progressive disease state of the organic structure [29] (Table 6).

The fibrotic tissue produces mechanical forces that create traction effects on the airways, which serve as one of the bases for the development of bronchiectasis [30]. These studies on tracheal dilatation are consistent with this mechanism in which the stiffer tissue leads and modifies lung mechanics that directly affect the airway structure. Furthermore, vascular remodeling in IPF is known to affect airway architecture by modifying the peribronchial blood flow and tissue oxygenation [31] (Table 6).

There are noteworthy limitations that must be both understood and considered in the context of this analysis. The data that was obtained does not seem to be particularly robust and the sample size corresponds to $n = 86$. The sample also appears to be rather homogenous which may affect the statistical power obtained, especially in terms of subgroup analyses. The nature of our study is holistic in a way that it appears retrospective, and that can lead to biases such as selection bias, and information bias as a result of relying on pre-existing medical records. Complete data coverage probably was not possible due to several blanked out or incomplete records, which would have adversely affected the coverage admissible for certain variables. Furthermore, single-centered or monocentered approaches greatly reduce, if not eliminate, generalizability since the findings extracted may not cut across specific geography or demographic constraints. The temporality of the collected data cross sectionally denotes frequency polygons, thus limiting the ability to trace relationships and changes in trachea variables through time. In addition, any measurement deviation in the HRCT as well as the pulmonary function tests, irrespective of having a standardized set of protocols, may have an impact on the accuracy of results. These limitations should be improved upon, and addressed, through more prospective multicenter designs that do follow these protocols and have sufficient sample size along with prolonged and consistent monitoring. Help from several assessors is necessary for radiological inter-observer measurement with thorough scrutiny in the area, would, to a consider, excuse this area of concern. Whatever the case may be, another huge source of information that needs to be consolidated are any possible lurking factors like other medications, the nutrition, and other genetic makes which this study did not account for.

Conclusion

The aim of this study was to examine how the sizes and surface areas of the trachea and main bronchi relate, to the severity of illness and lung function in individuals, with Idiopathic Pulmonary Fibrosis (IPF). Results indicated that the trachea diameters and areas particularly those at the subcricoid region exhibited a positive correlation with GAP index. Likewise, the carina area also exhibited a satisfactory correlation with the GAP index. Interestingly, subcricoid and carina areas also exhibited a positivity with the FVC/DLCO ratio. A similar trend was also seen with the main bronchial areas especially the right main bronchial area which had a significant correlation with GAP index. However, there was no strong positive relationship found regarding FVC and DLCO with trachea and bronchus measurements. This suggests the possibility that trachea and bronchus measurements may be employed to evaluate the characteristics of the IPF disease but they should not have a significant influence on the pulmonary functions of IPF patients.

Abbreviations

IPF	Idiopathic Pulmonary Fibrosis
HRCT	High-resolution computed tomography
PFTs	Pulmonary function tests
FVC	Force vital capacity
DLCO	Diffusion capacity for carbon monoxide
GAP	The gender, age, physiology index
AP	Anteroposterior
FOV	Field of view
UIP	Usual interstitial pneumonia

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Author contributions

N.F. contributed to the conception, study design, execution, interpretation, analysis, and manuscript preparation, H.S. contributed to execution, acquisition of data, M.F. contributed to the data collection and manuscript revision. E.P.C. contributed to the data collection. L.C.M. contributed to analysis, interpretation. All authors reviewed the manuscript.

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Data availability

The datasets of the current study are available from the corresponding author upon reasonable request.

Declarations

Ethics approval and consent to participate

This study was approved by the ethical community of Tekirdag Namik Kemal University. We confirmed that all methods were performed in accordance with relevant guidelines and regulations to protect human subjects.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

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