Research Article

Pamukkale Medical Journal
doi:https://dx.doi.org/10.31362/patd.1804028

Evaluation of Diffusing Capacity for Carbon Monoxide (DLCO) and DLCO/VA (KCO) Across Different Lung Disease Phenotypes

Restriktif Akciğer Hastalıklarında Karbon Monoksit Difüzyon Kapasitesi (DLCO) ve Transfer Katsayısı (KCO): klinik değerlendirme ve yorumlama

Nilüfer Yiğit, Gizem Sönmez Urfan, Hande Şenol, Göksel Altınışık

Received:17.10.2025 Accepted:26.11.2025

Abstract

Purpose: Pulmonary function tests (PFTs) and diffusion capacity measurements, particularly DLCO and KCO (DLCO/VA), are essential for evaluating gas exchange impairment in various lung diseases. While DLCO reflects overall diffusion capacity, KCO may better discriminate between different pathophysiological mechanisms, especially in restrictive and obstructive lung disorders.

Materials and methods: This retrospective, observational case-control study included 100 patients over 18 years of age followed at our clinic between January 2019 and June 2024 with complete PFT and DLCO data. Patients were divided into four groups: idiopathic pulmonary fibrosis (IPF, n=25), hypersensitivity pneumonitis (HSP, n=25), emphysema-dominant COPD (n=25), and chronic pleuroparenchymal fibroelastosis (KPFA, n=25). Groups were balanced by consecutively including patients after identifying 25 newly diagnosed IPF cases.

Results: Mean DLCO values were reduced across all groups (42-51%), with no statistically significant differences (p=0.182). In contrast, KCO values differed significantly among groups (p<0.001), with emphysema patients showing markedly lower KCO compared to IPF and HSP groups, reflecting impaired gas exchange efficiency per unit alveolar volume. TLC values did not differ significantly (p=0.165), while spirometric parameters demonstrated characteristic obstructive patterns in emphysema and relatively preserved values in fibrotic diseases. These findings highlight the importance of assessing KCO alongside DLCO and VA to better distinguish between parenchymal and extraparenchymal restrictive disorders.

Conclusion: While DLCO alone cannot reliably differentiate lung disease subtypes, KCO provides a more sensitive measure of underlying pathophysiology. By supporting previously reported and sometimes controversial literature values with real-world patient data, this study contributes meaningful evidence to the clinical interpretation of diffusion parameters. Integrating KCO, DLCO, and VA measurements enhances diagnostic accuracy and understanding of gas exchange abnormalities across distinct lung diseases.

Keywords: Diffusing capacity for carbon monoxide (DLCO), transfer coefficient (KCO), interstitial lung disease (ILD), emphysema, pulmonary function testing.

Yigit N, Sonmez Urfan G, Senol H, Altinisik G. Evaluation of Diffusing Capacity for Carbon Monoxide (DLCO) and DLCO/VA (KCO) Across Different Lung Disease Phenotypes. Pam Med J 2026;19:109-117.

Öz

Amaç: Solunum fonksiyon testleri (SFT) ve difüzyon kapasitesi ölçümleri, özellikle DLCO ve KCO (DLCO/VA), çeşitli akciğer hastalıklarında gaz değişim bozukluğunu değerlendirmede hayati öneme sahiptir. DLCO genel difüzyon kapasitesini yansıtırken, KCO farklı patofizyolojik mekanizmaları ayırt etmede özellikle restriktif ve obstrüktif akciğer hastalıklarında daha belirleyici olabilir.

Gereç ve yöntem: Bu retrospektif, gözlemsel olgu-kontrol çalışmasına Ocak 2019–Haziran 2024 tarihleri arasında kliniğimizde izlenen ve SFT ile DLCO verileri eksiksiz olan 18 yaş üstü 100 hasta dahil edilmiştir. Hastalar dört gruba ayrılmıştır: idiyopatik pulmoner fibrozis (İPF, n=25), hipersensitivite pnömonisi (HSP, n=25), amfizem baskın KOAH (n=25) ve kronik plevroparankimal fibroelastozis (KPFA, n=25). Gruplar, 25 yeni tanı almış İPF olgusunun belirlenmesinin ardından ardışık hasta dahil edilerek dengelenmiştir.

Bulgular: Ortalama DLCO değerleri tüm gruplarda azalmış olup (%42-51) istatistiksel olarak anlamlı farklılık göstermemiştir (p=0,182). Buna karşın, KCO değerleri gruplar arasında anlamlı şekilde farklı bulunmuştur (p<0,001); amfizemli hastalarda KCO, İPF ve HSP gruplarına göre belirgin şekilde düşük olup, alveoler hacim başına azalmış gaz değişim verimliliğini yansıtmaktadır. TLC değerleri gruplar arasında anlamlı farklılık göstermemiştir (p=0,165), ancak spirometrik parametreler amfizem grubunda tipik obstrüktif paterni gösterirken fibrotik hastalıklarda nispeten korunmuş değerler saptanmıştır.

Nilüfer Yiğit, Asst. Prof. Pamukkale University Faculty of Medicine, Department of Chest Diseases, Denizli, Türkiye, e-mail: nyigit@pau.edu.tr (https://orcid.org/0000-0002-5871-6461) (Corresponding Author)

Gizem Sönmez Urfan, M.D. Pamukkale University Faculty of Medicine, Department of Chest Diseases, Denizli, Türkiye, e-mail: gsonmez@pau.edu.tr (https://orcid.org/0009-0006-0568-4474)

Hande Şenol, Asst. Prof. Pamukkale University Faculty of Medicine, Department of Biostatistics, Denizli, Türkiye, e-mail: hsenol@pau.edu.tr (https://orcid.org/0000-0001-6395-7924)

Göksel Altınışık, Prof. Pamukkale University Faculty of Medicine, Department of Chest Diseases, Denizli, Türkiye, e-mail: galtınısık@pau.edu.tr (https://orcid.org/0000-0001-6869-1301)

Bu bulgular, DLCO ve VA ile birlikte KCO değerlendirilmesinin parankimal ve ekstraparankimal restriktif bozuklukların ayrımında önemini vurgulamaktadır.
Sonuç: DLCO tek başına akciğer hastalığı alt tiplerini güvenilir şekilde ayırt edemezken, KCO altta yatan patofizyolojiyi daha hassas olarak yansıtmaktadır. Literatürde hali hazırda bilinen ve tartışmalı değerleri, gerçek hasta verileri ile destekleyerek klinik yorumlamaya katkı sağlamaktadır. KCO, DLCO ve VA ölçümlerinin birlikte değerlendirilmesi, farklı akciğer hastalıklarındaki gaz değişim bozukluklarının anlaşılmasını ve tanısal doğruluğu artırmaktadır.

Anahtar kelimeler: Karbon monoksit difüzyon kapasitesi (DLCO), Transfer katsayısı (KCO veya DLCO/VA), amfizem, interstisyel akciğer hastalığı (İAH), solunum fonksiyon testi.

Yiğit N, Sönmez Urfan G, Şenol H, Altınışık G. Restriktif Akciğer Hastalıklarında Karbon Monoksit Difüzyon Kapasitesi (DLCO) ve Transfer Katsayısı (KCO): klinik değerlendirme ve yorumlama. Pam Tıp Derg 2026;19:109-117.

Introduction

Pulmonary function tests (PFTs) are indispensable diagnostic tools in the evaluation, classification, and follow-up of pulmonary diseases. These tests provide essential information for distinguishing between obstructive and restrictive pathologies. They are particularly important in assessing disease severity and monitoring treatment response in conditions such as chronic obstructive pulmonary disease (COPD), asthma, interstitial lung diseases, and restrictive disorders of neuromuscular origin [1, 2].

Among the various PFT methods, simple spirometry is the most used technique. It assesses airflow limitation through parameters such as FEV_1 (Forced Expiratory Volume in one second), FVC (Forced Vital Capacity), FEV_1/FVC ratio, and PEF (Peak Expiratory Flow). Spirometry is frequently preferred as an initial diagnostic test due to its low cost, non-invasive nature, and ease of application [3]. However, while spirometry evaluates airflow-related abnormalities, it does not provide information about gas exchange capacity. Therefore, it may be insufficient for diagnosing parenchymal processes such as interstitial lung diseases.

Tests evaluating gas transfer capacity have been developed to complement spirometry in assessing parenchymal lung disease, with the diffusing capacity for carbon monoxide (DLCO) being the most widely used parameter. DLCO measures the ability of carbon monoxide (CO) to diffuse across the alveolocapillary membrane into the pulmonary capillaries, providing direct insight into pulmonary gas exchange function. Test results are influenced by multiple factors, including the integrity of the alveolocapillary membrane, pulmonary capillary blood flow, hemoglobin level, and alveolar volume [4]. Consequently, accurate clinical interpretation of DLCO requires considering all these parameters together.

The DLCO value adjusted for alveolar volume (VA), known as DLCO/VA or the transfer coefficient (KCO), can provide more meaningful information, particularly in conditions accompanied by reduced lung volumes. In some restrictive lung diseases, DLCO may decrease while KCO remains within normal limits, suggesting extraparenchymal pathology (such as pleural, chest wall, or neuromuscular causes) rather than primary parenchymal disease [5, 6]. Careful interpretation of KCO is essential, however, as this parameter can sometimes yield misleading diagnostic results.

According to recent literature, the relationship between DLCO and VA is not linear, which may lead to misleading interpretations of DLCO/VA [2, 4, 7]. The nonlinear relationship between DLCO and lung volume prevents DLCO/VA from serving as a true correction factor for DLCO when lung volumes are reduced [7]. Therefore, interpretation of DLCO/VA requires caution, particularly in the presence of decreased alveolar volume. For instance, if a reduction in alveolar volume is accompanied by a proportional decrease in DLCO, a normal KCO may give a misleading impression that gas exchange capacity is preserved [8]. Therefore, studies that support the interpretation and diagnostic value of these parameters with real-world data are needed. Building on this need, the present study aims to comparatively evaluate changes in DLCO, VA, and KCO across different lung

disease groups and to contribute to clarifying the uncertainties in their clinical interpretation. We hypothesize that evaluating KCO together with DLCO and alveolar volume (VA) provides a more accurate distinction between different pathophysiological mechanisms in lung diseases than assessing DLCO alone. By examining the effects of different pathophysiological mechanisms on these parameters, we aim to emphasize the importance of accurate interpretation of KCO in clinical practice, since it may facilitate a more precise distinction between parenchymal and extraparenchymal restrictive lung diseases and help prevent misinterpretations. By examining the effects of different pathophysiological mechanisms on DLCO and KCO, we aim to emphasize the importance of accurately interpreting KCO in clinical practice. This approach may contribute to a more precise distinction between parenchymal and extraparenchymal restrictive diseases and help prevent misinterpretations. Since DLCO and KCO can be misleading when evaluated in isolation, it is important to consider lung volume measurements such as VA and TLC when interpreting these parameters. Increasing the use of body box measurements for TLC assessment in clinical practice would allow for more reliable evaluations. Furthermore, interpreting these functional data in conjunction with thoracic CT/HRCT findings would provide stronger support for definitive diagnostic decisions.

Materials and methods

This retrospective, observational case-control study included patients over 18 years of age who were followed in our pulmonary diseases clinic between January 2019 and June 2024 and had complete PFT and DLCO data. Since no comparable study exists in the literature, a priori power analysis assuming a moderate effect size (F=0.4) indicated that inclusion of at least 76 participants (19 per group) would provide 80% power at a 95% confidence level. Accordingly, the study population was divided into four groups: idiopathic pulmonary fibrosis (IPF), hypersensitivity pneumonitis (HP), COPD with an emphysematous pattern, and combined pulmonary fibrosis and emphysema (CPFE). Within this period, 25 newly diagnosed IPF patients with complete data were identified, and 25 consecutively evaluated patients meeting inclusion criteria were selected from each of the other groups, yielding 100 patients in total.

Study population

During the follow-up period, patients with confirmed diagnoses were included as follows: IPF diagnosed according to current guidelines based on HRCT and/or histopathological findings consistent with usual interstitial pneumonia; COPD confirmed by spirometric obstruction (FEV_1/FVC <70%) with clinical and radiological evidence of emphysema; CPFE characterized by the coexistence of fibrotic and emphysematous changes; and HP diagnosed based on compatible clinical, radiological, and/or histopathological findings.

The inclusion criterion required at least one valid PFT and DLCO measurement for each patient.

Measurements were excluded if they were deemed technically invalid (not meeting ATS/ERS quality criteria for spirometry or DLCO), obtained during an episode of acute exacerbation, active pulmonary infection, or recent pulmonary embolism (i.e., outside of a stable clinical period), or if hemoglobin data were unavailable when DLCO correction was required.

Statistical analysis

All statistical analyses were performed using SPSS 25.0 software (IBM SPSS Statistics 25 software (Armonk, NY: IBM Corp.)). Continuous variables were expressed as mean ± standard deviation and categorical variables as number and percent. The Shapiro–Wilk test was used for testing normality. If parametric test conditions were satisfied, one-way analysis of variance (post hoc: Tukey test) was used for comparisons among groups. If parametric test conditions were not satisfied, the Kruskal–Wallis test (post hoc: Mann Whitney U-test with Bonferroni correction) was used for comparisons among groups. The chi-square test was used to compare the categorical variables. <0.05 was considered statistically significant. This study was carried out in accordance with the Helsinki Declaration and was approved by the Pamukkale University Non-Interventional Clinical Research Ethics Committee (approved date: October 22, 2024; approved decision no: 18).

Results

A total of 100 patients were retrospectively included in our study and divided into four equal groups according to their diagnoses. Group 1 (n=25), 8 patients (32%) were female, and the mean age was 73.88 years. Group 2 (n=25), with 10 females (40%) and a mean age of 65.28 years. Group 3 (n=25) had only 1 female patient (4%) and a mean age of 67.48 years. Finally, Group 4 (n=25), of whom 4 (16%) were female, with a mean age of 65.50 years. The demographic and basic clinical characteristics of patients are presented in Table 1.

Table 1. Demographic and clinical characteristics of the study groups

Variable	Group 1	Group 2	Group 3	Group 4	*p*-value	Significant pairwise comparisons
Age (years, mean ± SD)	73.88±11.1	65.28±14.7	67.48±6.97	65.50±10.64	0.016* (kw=10.281)	1-4.
Sex, n (%)						
Female	8 (33.3)	10 (40.0)	1 (4.0)	4 (16.7)	0.012* (cs=10.998)	1-3, 2-3
Male	17 (66.7)	15 (60.0)	24 (96.0)	21 (83.3)		
Smoking status, n (%)						
Never smoked	54.2	48.0	4.0	16.7		
Current smoker	45.8	20.0	88.0	50.0	0.0001* (cs=37.002)	1-3, 1-4, 2-3
Ex-smoker	0.0	32.0	8.0	33.3		
Smoking exposure (pack-years, mean ± SD)	16.96±20.66	16.96±21.42	53.96±27.64	36.21±22.51	0.0001* (kw=29.079)	1-3, 2-3

*$p<0.05$ was considered statistically significant. kw: Kruskal Wallis Variance Analysis, F: One Way Analysis of Variance

No statistically significant differences were observed in DLCO values among the groups ($p=0.182$). The mean DLCO was 48.75±21.24 in Group 1, 51.28±19.11 in Group 2, 42.48±26.92 in Group 3, and 43.29±16.10 in Group 4. DLCO values were below 80% in all groups, indicating a marked reduction in diffusion capacity. When comparing fibrotic-dominant diseases (Group 1: UIP and Group 2: HP) with emphysema-dominant diseases (Group 3: emphysema and Group 4: KPFA), diffusion capacity remained low across both categories.

Significant differences were observed in KCO values among the groups ($p<0.001$). The mean KCO values were 79.63±22.93 (median 75, range 32-121) in Group 1, 89.2±30.47 (median 94, range 38-187) in Group 2, 56±21.46 (median 51, range 23-103) in Group 3, and 63.88±21.09 (median 64, range 21-102) in Group 4. Pairwise comparisons revealed that Group 3 had significantly lower KCO values compared to Groups 1 and 2, and a significant difference was also observed between Groups 2 and 4 ($p<0.05$) (Table 2).

Spirometry parameters showed a significant difference in Group 3. The FEV_1/FVC ratio was 81.42±7.05 in Group 1, 79.4±6.54 in Group 2, and 74.29±10.02 in Group 4, while it was 42.2±9.68 in Group 3, representing a statistically significant decrease ($p<0.001$) (Table 2)

FEV_1 and FVC parameters were evaluated, revealing that FEV_1 values in Group 1 and Group 2 were within the normal range. A statistically significant difference was observed among FEV_1 values ($p<0.001$). The mean FEV_1 was 89.5±15.37 in Group 1, 76.72±16.55 in Group 2, 32.92±14.16 in Group 3, and 79.75±22.16 in Group 4. Pairwise comparisons showed that the mean FEV_1 in Group 3 was significantly lower than in the other groups (Table 2).

A statistically significant difference was also observed among FVC (forced vital capacity) values (p<0.001). The mean FVC was 86.54±18.13 in Group 1, 76.32±15.85 in Group 2, 59.2±15.38 in Group 3, and 82.88±19.31 in Group 4. The mean FVC in Group 3 was significantly lower compared to Groups 1, 2, and 4 (p<0.001) (Table 2).

Table 2. Pulmonary function test (PFT) parameters among study groups

Parameter	Group 1	Group 2	Group 3	Group 4	*p*-value
DLCO (%predicted)	48.75±21.24	51.28±19.11	42.48±26.92	43.29±16.10	0.182 (kw=4.87)
KCO (DLCO/VA, % predicted)	79.63±22.93	89.20±30.47	56.00±21.46	63.88±21.09	0.0001* (kw=22.301)
TLC (% predicted)	59.63±12.44	60.36±15.44	60.04±20.12	69.04±18.37	0.165 (F=1.738)
FEV_1 (% predicted)	89.50±15.37	76.72±16.55	32.92±14.16	79.75±22.16	0.0001* (kw=54.153)
FVC (% predicted)	86.54±18.13	76.32±15.85	59.20±15.38	82.88±19.31	0.0001* (F=12.221)
FEV_1 / FVC (%)	81.42±7.05	79.40±6.54	42.20±9.68	74.29±10.02	0.0001* (kw=58.095)

Values are expressed as mean ± standard deviation (SD), *p<0.05 was considered statistically significant, TLC: total lung capacity DLCO: diffusing capacity for carbon monoxide; KCO: transfer coefficient (DLCO/VA), FEV_1: forced expiratory volume in one second FVC: forced vital capacity, kw: Kruskal Wallis Variance Analysis; F: One Way Analysis of Varince

Discussion

Diffusion impairment is a common feature across many parenchymal lung diseases; the extent and pattern of this impairment may vary substantially depending on the underlying pathology [9]. In our cohort, all patient groups exhibited similarly reduced DLCO values, indicating a generalized limitation in alveolar-capillary diffusion. However, KCO revealed striking differences, being markedly decreased in emphysema while remaining relatively preserved in fibrotic subtypes such as UIP and HP. Moreover, despite comparable TLC values across groups, pronounced variations in KCO and VA highlighted the dissociation between lung volume and gas exchange efficiency. These findings emphasize that DLCO alone may underestimate disease-specific physiological alterations, whereas KCO when interpreted alongside alveolar volume can provide a more refined reflection of underlying pathophysiology.

DLCO and KCO measurements have long been used to assess impairments in gas exchange. However, there are differing opinions and conflicting interpretations regarding the clinical use of KCO [2, 5, 10]. For instance, patients with low lung volumes, including those with interstitial lung disease or extraparenchymal restrictive disorders (e.g., kyphoscoliosis), DLCO/VA expressed as a percentage of predicted values often exceeds DLCO. While some authors interpret these findings in relation to the underlying lung pathology [11, 12], others accept that these discrepancies largely stem from limitations in the predictive equations [10, 13]. Therefore, our study aimed to evaluate how DLCO and KCO values vary among different subtypes of interstitial lung diseases, COPD with concomitant emphysema, and CPFE by using real-world data, and to contribute to the combined interpretation of these parameters in clinical practice. Our findings revealed that although all patient groups exhibited a marked reduction in diffusion capacity, KCO values were significantly lower in emphysematous patients, whereas they remained relatively preserved in fibrotic subtypes. Moreover, despite comparable TLC values across groups, the pronounced differences observed in KCO and alveolar volume suggest that disease-specific mechanisms play a distinct role in the physiology of gas exchange.

In the current study, no statistically significant differences were observed in DLCO values among the four patient groups. DLCO levels below 80% across all groups indicate a marked reduction in diffusion capacity. This finding aligns with previous reports suggesting that both interstitial fibrotic changes and emphysematous structural alterations limit the alveolar-capillary surface area, resulting in diffusion impairment [1, 14]. However, reduced DLCO alone appears insufficient to differentiate between these patient subtypes. Several studies have reported that while DLCO reflects overall lung damage, it has limited discriminative value in identifying the fibrotic versus emphysematous nature of the underlying pathology [7, 15]. This limitation highlights the importance of including volume-normalized parameters, such as KCO, to enhance clinical interpretability, as supported by the findings of the current study.

Notably, KCO, being adjusted for VA, more accurately reflects gas exchange efficiency and allows for a clearer assessment of the effects of different pathological mechanisms. This enhances the utility of KCO in distinguishing between various conditions, such as interstitial lung diseases and emphysema [1, 7]. In the current analysis, KCO values differed significantly among the groups. Specifically, marked differences were observed between Group 3 (emphysema) and both Group 1 (UIP) and Group 2 (HP), highlighting the discriminative power of KCO in differentiating disease subtypes. These findings suggest that KCO provides a more sensitive measure of gas exchange efficiency, contributing to a better understanding of underlying pathophysiological mechanisms.

There are detailed reports explaining the pathophysiological basis of DLCO and KCO and guidance on their interpretation. However, some studies evaluate emphysema and interstitial lung diseases together in one group, which can complicate the interpretation of subgroups in clinical practice [7]. In certain cases, adjusting KCO for VA does not always provide additional clinically relevant information and may be overemphasized [5]. These observations underscore the limitations of interpreting KCO in isolation, particularly in patients with ventilation inhomogeneity or altered lung volumes. Accordingly, studies supported by real-world data are essential. By analyzing DLCO and KCO values across four well-defined patient groups using real-world data, the current study provides insight into the clinical value of KCO in differentiating these subgroups.

Alveolar volume reflects the total lung volume available for gas exchange and is affected differently across various pathological processes. In emphysema, destruction of alveolar structures and expansion of airspaces typically lead to increased VA; consequently, while DLCO is reduced, KCO may be more markedly decreased, as the gas exchange efficiency per unit alveolar volume is diminished. Conversely, in interstitial lung diseases, particularly fibrotic subtypes, lung parenchyma becomes stiff, and volume loss occurs; VA decreases, and DLCO is reduced, but KCO is often normal or high-normal, as the remaining alveoli continue to perform relatively efficient gas exchange [16].

This distinction highlights that DLCO alone has limited capacity to differentiate between these pathologies, whereas KCO, adjusted for AV, provides a more informative parameter for discriminating pathological subgroups. In our study, DLCO values were consistently below 80% across all four patient groups, indicating marked diffusion impairment in all cases. However, when evaluating KCO, the adjustment for VA revealed pronounced differences, particularly between the emphysema group and patients with interstitial lung diseases (UIP and HP). These findings demonstrate that while DLCO alone cannot reliably distinguish between subgroups, VA-adjusted KCO more accurately reflects underlying pathophysiological differences and changes in gas exchange efficiency.

In recent years, the literature has emphasized the importance of evaluating the VA/TLC ratio alongside DLCO in distinguishing subgroups of restrictive and obstructive lung diseases [7]. In cases of reduced DLCO, the ratio of VA to TLC emerges as a clinically valuable parameter for determining whether alveolar volume loss is related to a parenchymal or extraparenchymal mechanism. This approach is particularly helpful in understanding the mechanism of diffusion impairment and preventing misinterpretation in subgroups such as fibrotic interstitial lung diseases and emphysema [8].

Our study was designed retrospectively, and TLC data obtained through gold-standard techniques such as body box measurements were not available. Therefore, direct data regarding this parameter cannot be provided. In future prospective studies, emphasizing these measurements would be meaningful.

When spirometry parameters were examined, a pronounced obstructive pattern was observed in the emphysema group. The significantly reduced FEV_1/FVC ratio reflects typical obstructive pathophysiology in these patients, characterized by small airway narrowing and airflow limitation. This finding is clinically consistent with conditions in which air trapping predominates, such as emphysema or COPD [17]. Indeed, the relatively higher TLC values in this patient group support the contribution of hyperinflation and air trapping [18]. Correspondingly, the marked reduction in DLCO and particularly KCO values can be explained by the loss of alveolar surface area, which diminishes gas exchange capacity [5]. Therefore, evaluating the obstructive pattern in spirometry measurements alongside impaired diffusion parameters enhances diagnostic accuracy, especially in cases accompanied by emphysematous destruction [19].

The marked difference in FEV_1 values between the groups is particularly notable in the emphysema group, where significantly lower mean values were observed. This finding aligns with the characteristic features of emphysema, including airway collapse, loss of elastic recoil, and air trapping, which lead to reduced expiratory flow rates [1]. In contrast, FEV_1 values in the UIP group and HP group, representing interstitial lung diseases, largely remained within normal ranges, reflecting a restrictive pattern that manifests predominantly as reduced lung volumes. Therefore, from a spirometry perspective, decreased FEV_1 serves as a clear indicator of an obstructive pattern, illustrating the functional impact of alveolar destruction in the emphysema group. Moreover, when considered alongside the low FEV_1/FVC ratio and reduced KCO values observed in this group, these findings support the impact of structural impairments at both the airway and alveolar levels on gas exchange [5, 19].

Regarding FVC values, a significant decrease was observed in emphysema, whereas FVC values in UIP, HP, and CPFE were relatively preserved. Although a reduction in FVC is generally expected in fibrotic interstitial lung diseases, the maintenance of FVC within normal ranges in our study is notable, likely reflecting the early stage of disease in these patients who had recently received a diagnosis and were initiated into treatment. Therefore, in the early phases of fibrotic disease, normal FVC values may be observed in pulmonary function tests, while more pronounced declines, particularly in DLCO and other diffusion parameters, may appear as the disease progresses. In contrast, patients with emphysema may exhibit significant reductions in both FVC and DLCO even in the early stages due to alveolar destruction and air trapping. These differences highlight the distinct pathophysiological processes underlying each disease group and underscore the importance of considering disease stage when interpreting pulmonary function tests.

This study has several limitations that should be acknowledged. First, its retrospective and single-center design may limit the generalizability of the findings, as patient selection and diagnostic practices could differ across centers. Second, the sample size in each subgroup was relatively small, which may have reduced the statistical power for detecting subtle intergroup differences. Third, TLC and VA/TLC data obtained through body plethysmography were not available, precluding a more detailed analysis of lung volume–diffusion relationships. Finally, as this was a cross-sectional analysis, longitudinal changes in diffusion parameters and their response to treatment could not be evaluated.

Despite these limitations, the study provides valuable real-world data and contributes to clarifying the clinical interpretation of DLCO and KCO across different lung disease phenotypes.

In conclusion, our study evaluated the discriminative characteristics of DLCO and KCO parameters across different lung diseases. The findings demonstrate that DLCO was similarly reduced in all groups, whereas KCO showed a marked decrease, particularly in patients with

emphysema. The preservation of FVC in early-stage fibrotic cases reflects the impact of disease stage on pulmonary function parameters. Since the presence of certain controversial aspects in the literature underscores the need for support from real-world data, the current study provides clinically observed data that complement the existing literature and clarify the relationship between diffusion physiology and different disease patterns. Although the number of patients in each subgroup was relatively limited, the inclusion of well-defined and consecutively selected cases allowed for meaningful comparisons among distinct parenchymal disease patterns. Therefore, despite its sample size constraints, this study offers valuable insight into the differential behavior of DLCO and KCO across various pulmonary pathologies.

Funding: None.

Authors contributions: N.Y. constructed the main idea and hypothesis of the study. N.Y., G.S. H.S. developed the theory and arranged/edited the material and method section. H.S. has done the evaluation of the data in the results section. The Discussion section of the article was written by N.Y., G.S., G.A. reviewed, corrected and approved. In addition, all authors discussed the entire study and approved the final version.

Conflict of interest: No conflict of interest was declared by the authors.

References

1. Pellegrino R, Viegi G, Brusasco V, et al. Interpretative strategies for lung function tests. *Eur Respir J*. 2005;26(5):948-968. doi:10.1183/09031936.05.00035205
2. Graham BL, Steenbruggen I, Miller MR, et al. Standardization of Spirometry 2019 Update. An Official American Thoracic Society and European Respiratory Society Technical Statement. *Am J Respir Crit Care Med.* 2019;200(8):e70-e88. doi:10.1164/rccm.201908-1590ST
3. Wanger J, Clausen JL, Coates A, et al. Standardisation of the measurement of lung volumes. *Eur Respir J*. 2005;26(3):511-522. doi:10.1183/09031936.05.00035005
4. Macintyre N, Crapo RO, Viegi G, et al. Standardisation of the single-breath determination of carbon monoxide uptake in the lung. *Eur Respir J*. 2005;26(4):720-735. doi:10.1183/09031936.05.00034905
5. Hughes JM, Pride NB. Examination of the carbon monoxide diffusing capacity (DL(CO)) in relation to its KCO and VA components. *Am J Respir Crit Care Med*. 2012;186(2):132-139. doi:10.1164/rccm.201112-2160CI
6. Myrberg T, Lindberg A, Eriksson B, et al. Restrictive spirometry versus restrictive lung function using the GLI reference values. *Clin Physiol Funct Imaging*. 2022;42(3):181-189. doi:10.1111/cpf.12745
7. Turkish Thoracic Society. *Interpretation of Pulmonary Diffusion Capacity: Consensus Report*. Ankara: Turkish Thoracic Society; 2022.
8. Stanojevic S, Graham BL, Cooper BG, et al. Official ERS technical standards: Global Lung Function Initiative reference values for the carbon monoxide transfer factor for Caucasians. *Eur Respir J*. 2017;50(3):1700010. doi:10.1183/13993003.00010-2017
9. Neder JA, Berton DC, Muller PT, O'Donnell DE. Incorporating Lung Diffusing Capacity for Carbon Monoxide in Clinical Decision Making in Chest Medicine. *Clin Chest Med*. 2019;40(2):285-305. doi:10.1016/j.ccm.2019.02.005
10. Johnson DC. Importance of adjusting carbon monoxide diffusing capacity (DLCO) and carbon monoxide transfer coefficient (KCO) for alveolar volume. *Respir Med*. 2000;94(1):28-37. doi:10.1053/rmed.1999.0740
11. Ayers LN, Ginsberg ML, Fein J, Wasserman K. Diffusing capacity, specific diffusing capacity and interpretation of diffusion defects. *West J Med*. 1975;123(4):255-264.
12. Kaminsky DA, Whitman T, Callas PW. DLCO versus DLCO/VA as predictors of pulmonary gas exchange. *Respir Med*. 2007;101(5):989-994. doi:10.1016/j.rmed.2006.09.003
13. Frans A, Nemery B, Veriter C, Lacquet L, Francis C. Effect of alveolar volume on the interpretation of single breath DLCO. *Respir Med*. 1997;91(5):263-273. doi:10.1016/s0954-6111(97)90029-9
14. Cottin V, Nunes H, Brillet PY, et al. Combined pulmonary fibrosis and emphysema: a distinct underrecognised entity. *Eur Respir J*. 2005;26(4):586-593. doi:10.1183/09031936.05.00021005
15. Devalla L, Ghewade B, Jadhav U, Annareddy S. Resolving the complexity: a comprehensive review on carbon monoxide diffusion capacity in chronic obstructive pulmonary disease patients. *Cureus*. 2024;16(2):e53492. doi:10.7759/cureus.53492
16. Goldin J, Cascella M. Diffusing Capacity of the Lungs for Carbon Monoxide. Wright State University School of Medicine; Istituto Nazionale Tumori - IRCCS - Fondazione Pascale, Napoli, Italy. Last update October 6, 2024.

17. Celli BR, Wedzicha JA. Update on Clinical Aspects of Chronic Obstructive Pulmonary Disease. *N Engl J Med*. 2019;381(13):1257-1266. doi:10.1056/NEJMra1900500
18. Global Initiative for Chronic Obstructive Lung Disease (GOLD) 2024 Report. *Global strategy for prevention, diagnosis and management of COPD.*
19. Macintyre N, Crapo RO, Viegi G, et al. Standardisation of the single-breath determination of carbon monoxide uptake in the lung. *Eur Respir J*. 2005;26(4):720-735. doi:10.1183/09031936.05.00034905