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Original Article

Evaluation of Speckle-Tracking Echocardiography in COPD Patients Without Comorbidities

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ABSTRACT

Background: Chronic obstructive pulmonary disease (COPD) and heart failure represent 2 entities of a growing global burden that share common clinical and etiological characteristics. Timely identification of heart failure is imperative for effective management. This study aimed to investigate subclinical left ventricular (LV) dysfunction by conventional and speckle-tracking echocardiography (STE) methods in COPD patients.

Methods: This is a prospective cohort study on 46 (54.1%) newly diagnosed patients with COPD without comorbidities (formerly diagnosed with confounders for evaluating cardiac performance: arrhythmias, diabetes, old age, hypertension, renal failure, and cardiovascular or valvular disease) (46.80±4.67 y, 30 (65.2%) males), and 39 (45.9%) age- and sex-matched healthy control smokers. COPD patients were classified based on the Global Initiative for Chronic Obstructive Lung Disease (GOLD) stages.

Results: Contrary to conventional echocardiographic parameters, STE revealed impairment of the LV basal circumferential strain (BCS) among COPD patients (-21.20%±3.89% vs -23.70±5.75; *P*=0.003) and gradually reduced with the severity of COPD GOLD (*P*=0.007), indicating LV dysfunction. Regarding global circumferential or longitudinal STE, COPD patients did not vary significantly (*P*=0.10, 0.57). In multiple linear regression analysis, spirometry parameters (FEV1(L), FEV%, FVC(L), FVC%, and FEV1/FVC) predicted BCS (*P*=0.023).

Right bundle branch block was observed more frequently (*P*=0.005) and the tricuspid annular plane systolic excursion level was significantly lower (*P*=0.017) among the COPD group. The results were associated with the degree of COPD GOLD severity (*P*=0.036), indicating right ventricular dysfunction.

Conclusions: COPD seems to be accompanied by impaired subclinical right ventricular and regional-level LV deformation properties that worsen in stages of COPD GOLD. ***(Iranian Heart Journal 2024; 25(2): 15-25)***

KEYWORDS: Echocardiography, Pulmonary disease, Chronic obstructive, Left ventricular dysfunction, Heart failure

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The natural course of chronic obstructive pulmonary disease (COPD) influences disorders beyond the lungs and is commonly associated with cardiovascular disease (CVD). [1,2] According to the World Health Organization statistical data, CVD is the first cause, and COPD is the third most prevalent cause of mortality worldwide. [3] COPD also represents an independent risk factor for CVD. [4] On the other hand, CVD is one of the principal determinants of COPD morbidity and mortality. The coexistence of COPD with heart failure (HF) is associated with a poor prognosis. Almost half of all deaths and hospitalizations related to COPD are linked to CVD. [5] Conventional echocardiographic studies have identified an association between advanced-stage COPD and biventricular dysfunction. [6] Even subclinical biventricular dysfunction is detectable in mild stages of COPD. [7] Mechanisms contributing to CVD in patients with COPD include oxidative stress, hypoxia, vascular endothelial dysfunction, chronic systemic inflammation, and smoking. [8] The conflation of symptoms in COPD and HF engenders a state of perplexity among clinicians, leading to ineffective treatment.

A study on patients with COPD, excluding those with a current diagnosis of HF, revealed that the prevalence of unrecognized HF was approximately 20%. [9] Furthermore, uncertainty about newly diagnosed CVD has also led to underusing CVD drugs, even in patients with known CVD. [10] Consequently, the treatment and management of diseases are often inadequate. [11] Appropriate treatment of CVD comorbidities can reduce mortality and economic burden. [12] Thus, detecting subclinical ventricular dysfunction is crucial in treating COPD and CVD.

Echocardiographic evaluation of left ventricular (LV) function in COPD is challenging, primarily due to lung hyperinflation but can be improved using the speckle-tracking echocardiography (STE)-based strain measurement of myocardial function. STE constitutes an established noninvasive imaging technique that enables visualization of ventricular strain and analysis of early-stage deformations. [13] STE demonstrates superior discriminatory power in assessing biventricular functions compared with conventional echocardiography. Therefore, an association has been found between the COPD BODE index (body mass index, airflow obstruction, dyspnea, and exercise capacity) and LV functions assessed by STE. [14]

As a result, this study hypothesized that COPD patients without other comorbidities might have subclinical LV dysfunction related to the severity stages of COPD. Thus, this study analyzed subclinical LV contractility status and geometric changes by conventional echocardiography and STE to determine the impact of concomitant COPD on cardiac contractility and to correlate the results with those obtained in matched control smokers.

METHODS

Study Population

The present prospective cohort study was conducted on 46 newly diagnosed outpatients with COPD at the pneumatological department between April 2022 and April 2023. The study included 39 age- and sex-matched healthy smoker controls. COPD diagnosis was confirmed by spirometry test results and clinical findings by the Global Initiative for Chronic Obstructive Lung Disease (GOLD) diagnostic criteria. [15] No airflow obstruction was detected among the controls. All confirmers, reviewers, and abstracters were blinded to the study. In total, 108 patients were examined, and 23 patients were excluded due to insufficient evidence of outcome events. All individuals with formerly diagnosed confounder

comorbidities (atrial fibrillation, conduction abnormalities, diabetes mellitus, old age [range =35–55 y), hypertension, renal failure, and valvular heart disease of a more-than-a-mild degree) for the evaluation of cardiac performance, low-quality echocardiographic images, malignancy, sleep-disordered breathing, or in case of COPD exacerbation within the preceding 3 months were excluded. None of the participants had any medication history or clinical evidence of HF.

In addition to COPD participants, smokers without prediagnosed comorbidities and lung function abnormalities were selected as the control group. The patients in the control group had normal spirometry test results. The control group was composed of current or previous smokers with a smoking history of more than 10 packs/year. Recruitment was from the general population by screening invitation.
Each study participant underwent an evaluation of cardiac performance status by 12-lead ECG, transthoracic echocardiography, offline LV-STE assessment, and laboratory testing before anti-obstructive or anti-inflammatory medication.

Evaluation of Pulmonary Function
Spirometry tests followed guidelines and were performed with the MIR Spirolab II (Rome/Italy) device. [16] The patients were informed about the maneuvers, and 3 spirograms were performed. The best results meeting the reproducibility and acceptability criteria were included in the study. The spirometry examination determined postbronchodilator forced expiratory volume in 1 second (FEV1), forced vital capacity (FVC), and the resulting FEV1 / FVC, 0.70, represented persistent airflow limitation and confirmed COPD. According to the guidelines, obstruction degrees of the spirometric examination, pneumatological symptomatology, and exacerbation risk factors defined COPD stages. [16]

Echocardiographic Analysis
Echocardiography was performed with an EPIQ 7C xMATRIX ultrasound system (Philips Healthcare, Bothell, WA, USA) with a 1-5 MHz X5-1 transducer probe. In the study population, LV dimensions, LV ejection fraction, and left atrial dimensions were measured, and complete 2D Doppler and tissue Doppler studies were performed. Data acquisition and imaging were carried out using the parasternal long-axis, parasternal short-axis, and apical 4-chamber views in the left lateral decubitus position and the subcostal view in the supine position while concurrently monitoring with 1-lead ECG.

2D-STE-Based LV Strain Assessment
To evaluate STE, LV views were recorded in grayscale using a frame rate of 60 to 70 frames per second, and 3 sequential cycles were acquired by holding the breath at the end of expiration. Echocardiographic recordings were digitized for further offline 2D STE analysis (Q-lab Advanced Quantification aCMQ software, version 10.4, Philips Medical Systems). Based on the grayscale apical 2-, 3-, and 4-chamber views, the LV endocardial border was manually traced from the septal to the lateral mitral ring and tracked over 2 cardiac cycles. The software automatically selected natural acoustic markers moving with the heart tissue. Regional LV longitudinal strain echocardiography (LSE) analysis was evaluated by separating the LV into 18 segments. LV global longitudinal strain echocardiography (GLSE) was calculated by mean values from all segments. Circumferential strain echocardiography (CSE) was measured in the view of the parasternal short axis. Regional CSE analysis separated the LV into 6 parts at apical, basal, and midventricular levels. The

maximal delays in the opposite segments were then measured. LV global circumferential strain echocardiography (GCSE) was calculated by mean values from all segments.

The study data were evaluated by double-blinded consultant cardiologists (at least post-fellowship experience of 10 years). For intraobserver variability assessment, recordings of 2D strain values were randomly selected from 10 participants and assessed by the same consultant cardiologist on different days. Intraobserver variability was evaluated by calculating the intraclass correlation coefficient. Values between 0.75 and 0.9 indicated good reliability, and values greater than 0.9 indicated excellent reliability. [17]

Definitions

Smoking history: Patients were divided into current cigarette smokers and past smokers: defined as those who had more than 6 months of abstinence from smoking and those who never smoked.

Ethics Statement

This study was performed in line with the principles of the Declaration of Helsinki. The approval was granted by the local S.H.E.H. Ethics Committee (Protocol No: 2309). All participants gave written informed consent.

Statistical Analysis

The Statistical Package for the Social Sciences (SPSS 17.0, IBM Chicago, IL, USA) program was used for statistical analysis. The Kolmogorov-Smirnov test determined the normally distributed data, and the ANOVA test determined the homogeneity of the data. Means with ±standard deviation and medians with 25th-75th percentiles were employed to report continuous variables, and percentages were used to express categorical variables. The Pearson test examined the correlations of parametric data. The Spearman test examined the correlations of nonparametric data. Variance analysis identified different groups. The independent sample Student *t* test assessed mean comparisons. The Mann-Whitney *U* and Kruskal-Wallis *H* tests evaluated median comparisons. Categorical variables were analyzed with the Pearson χ^2 test. Analysis of variance was used to determine whether different groups differed from each other. Adjudicated outcomes were tabulated by COPD and the control group. Medians with interquartile ranges reported continuous variables, and percentages expressed categorical variables. A linear regression test assessed the effects on basal strain levels. A *P* value <0.05 and a 95% confidence interval were accepted for statistical significance.

RESULTS

This study prospectively enrolled 46 (54.1%) COPD-confirmed outpatients without other comorbidities to assess their cardiac performance. Thirty-nine (45.9%) control participants were matched with the COPD group regarding age and sex. Demographic characteristics, clinical data, laboratory findings, ECG, and conventional echocardiographic parameters of the study population are summarized in Tables 1, 2, and 3. The COPD and control groups were similar in age, sex, body surface area (BSA), vital signs, and all laboratory findings.

Concerning smoking habits, the COPD group smoking packs/year exposure (27.930±7.278 packs/year) was significantly higher than that of the control group (22.670±8.880 packs/year), t(82) = -2.987; *P*=0.004), which additionally collimated over GOLD stages (control group, and COPD GOLD A through E), (χ^2(3, N=85) = 14.946; *P* 0.002, with a mean rank smoking packs/year score of 32.850 for the control group, 44.800 for GOLD A, 59.440 for GOLD B, and 51.250 for GOLD E). As

expected from these findings, the values of the pulmonary function test (FEV1(L), predicted% FEV1, FVC(L), predicted% FVC, FEV1/FVC) were highly significantly different between the COPD and control groups (respectively, z= -5.958, -7.914, -392., -6.883, and -6.968 (each with $P \leq 0.001$) (Table 2). Additionally, there was a statistically highly significant difference in the spirometry parameters between COPD GOLD A through E and the control group (FEV1(L) H(3, *N*=85) =41.330, FEV1 %predicted H(3, N=85) =69,020, FVC(L) H(3, N=85) =19.089, FVC %predicted H(3, N=85) = 52.585, FEV1/FVC H(3, N=85) =52.812 (each with $P \leq 0.001$).

ECG exhibited normal sinus rhythm without early beats or rhythm disturbances in all cases. Twelve patients (14.1%) had an incomplete or complete right bundle branch block (RBBB). RBBB was more frequently observed among COPD patients (11 [23.9%]) compared with the control group (1 [2.6%]) (X^2(1, N=85)=7.934; *P*=0.005). Further, in the COPD cohort, the tricuspid annular plane systolic excursion (TAPSE) level was significantly lower (2.360±0.283 cm) than that in the controls (2.523 ±0.334 cm) (t(83)=2.428; *P*=0.017). Likewise, diastolic LV performance lacked significant intercohortal differences (*P*=0.176). None of the study population had more than stage I diastolic dysfunction. The regurgitant tricuspid jet could not determine the estimated systolic pressure of the pulmonary artery in all the subjects. The control groups' median diameters of the left atrium (3.210 cm [3.000–3.350), the right atrium (3.340 cm [3.200–3.460]) and the LV internal end-diastolic (4.340 cm [4.080–4.600]) diameters were significantly lower than the COPD patients' median left atrium (2.990 cm [2.710–3.320]), right atrium (3.140 cm [2.890–3.363]), and LV internal end-diastolic (4.130 cm [3.653–4.390]) diameters (respectively, z= -2.245, -3.238, and -2.721; *P*=0.025, *P*=0.001, and *P*=0.007). Moreover, right atrial diameters gradually decreased in controls and COPD GOLD A through E, H(3, N=85) =11.282 (*P*= 0.01).

Regarding the findings of the STE-based strain assessment, COPD led to a reduction in levels of the basal circumferential strain (BCS) (t(77)= -2.272; *P*=0.026). It even gradually weakened within the degree of COPD GOLD (H (3, N=79)=12.004 (*P*= 0.007). The COPD patients' global circumferential or longitudinal STE assessment did not significantly vary compared with the controls (respectively, *P*=0.098 and *P*=0.573) or throughout the COPD GOLD stages (*P*=0.127 and *P*=0.195). Predictors of LV systolic function in the patients were determined by multivariate analysis with BCS strain as dependent variables and pulmonary function parameters, age, BSA, RBBB rhythm, sex, diastolic dysfunction, pack-year smoked, TAPSE, and vital signs as independent variables. Multiple linear regression was calculated to predict the level of BCS based on smoking and parameters of pulmonary function test (FEV1(L), predicted% FEV1, FVC (L), predicted% FVC, and FEV1/FVC ratio). A significant regression equation was found (F(6. 71)=2.640 (*P*=0.023), with an R^2 of 0.182. The participants' predicted BCS was equal to -16.138+0.122 (smoking packs/year exposure) -3.105 (FEV1(L)) +0.081 (%predicted FEV1) +2.656 (FVC(L)) -0.156 (%predicted FVC) -0.046 (FEV/FVC) where smoking was measured as in packs/year, FEV1(L) and FVC(L) were measured as in liters, %predicted FEV1, and FVC and FEV1/FVC ratio were coded as in ratio. BCS increased by 0.122 for each pack/year of smoking, 0,081 for each FEV1 ratio, 2.656 for each FVC liter, and decreased by 3.105 for each FEV1 liter, 0.156 for each FVC ratio, and0.046 for each FEV1/FVC ratio. The smoking packs/year

and the pulmonary function parameters were significant predictors of BCS.

No global time to peak circumferential or longitudinal strain standard deviation difference was found between the COPD and controls (respectively; *P*=0.389, *P*=0.921).

Table 1: Comparison of Baseline Demographic, Clinical Characteristics, and Laboratory Findings According to the Presence and Severity of COPD

Parameter	COPD GOLD A	COPD GOLD B	COPD GOLD E	All Study Population	All COPD Patients	Control Group	*P value (COPD Group vs Controls)	**P value (COPD GOLD A Through E and Controls)
Subjects, n (%)	24 (28.2)	16 (18.8)	6 (7.1)	85 (100)	46 (54.1)	39 (45.9)		
Demographics								
Gender, male n (%)	15 (62.5)	12 (75)	3 (50)	54 (63.5)	30 (65.2)	24 (61.5)	0.725	0.691
Age (years)	48.500 (41.500-50.750)	46.500 (43.000-49.500)	47.500 (43.000-51.000)	46.090 ± 4.755	46.800 ± 4.670	45.260 ± 4.778	0.136	0.459
BSA (m^2)	1.899 (1.672-2.016)	1.852 (1.741-2.164)	1.757 (1.728-2.044)	1.918 ±0.246	1.878 ± 0.241	1.965±0.248	0.105	0.358
Heart rate (bpm)	74.000 (67.000-80.500)	76.500 (67.500-90.250)	77.500 (74.500-90.750)	76.810 ±12.726	78.370 ±14.310	74.970 ±10.444	0.222	0.548
SBP (mm Hg)	119.500 (114.000-124.000)	124.000 (118.500-131.25)	121.00 (110.000-129.250)	122.530 ± 7.802	121.430 ±7.690	123.820 ±7.833	0.161	0.131
Smoking habits, n (%)							0.169	0.099
Current smoker	20 (83.3)	16 (100)	6 (100)	81 (95.3)	42 (91.3)	39(100.0)		
Former smoker	3 (12.5)	0 (0)	0 (0)	3 (3.5)	3 (6.5)	0 (0.0)		
Never smoker	1(4.2)	0 (0)	0 (0)	1 (1.2%)	1 (2.2)	0 (0.0)		
Smoking pack-year history	27.000 (20.000-30.000)	29.000 (26.000-36.000)	30.000 (19.500-34.250)	25.490 ± 8.436	27.930± 7.278	22.670±8.880	0.004†	0.002†
Laboratory Testing								
Na (mmol/L)	139.500 (138.000-140.000)	140.000 (138.250-142.750)	139.500 (138.750-141.250)	139.720 ± 2.410	139.850 ± 2.449	139.560 ± 2.382	0.591	0.624
K (mmol/L)	4.315 (4.100-4.765)	4.290 (4.115-4.490)	4.385 (4.175-4.708)	4.391 ± 0.549	4.309 ± 0.617	4.488 ± 0.444	0.134	0.515
Creatinine (mg/dL)	0.730 (0.613-0,900)	0.805 (0.578-0.900)	0.730 (0.660-0.823)	0.763 ± 0.150	0.755 ± 0.155	0.772 ± 0.145	0.592	0.901
Fasting glucose (mg/dL)	94.500 (83.250-101.000)	90.250 (88.250-98.000)	91.250 (82,250-100.500)	92.460 ± 10.042	92.860 ± 10.412	92.000 ± 9.701	0.697	0.973
AST (U/L)	18.500 (16.250-24.750)	16.500 (14.930-20.500)	15.000 (13.750-23.000)	18.000 (15.000 – 24.000)	17.500 (15.000-24.000)	19.940 ± 6.610	0.884	0.532
ALT (U/L)	17.500 (12.250-22.750)	15.00 (12.000-24.750)	17.000 (14.500-21.000)	18.000 (13.000 – 24.000)	17.000 (12.750-23.000)	21.48 ± 9.182	0.244	0.706
Leukocytes (10^9/mL)	8.360 (7.093-9.990)	8,855 (7.923-9.693)	9.220 (6.478-11.250)	8.220 ± 1.801	8.516 ± 1.901	8.276 ± 1.697	0.547	0.679
Hemoglobin (g/dL)	14.800 (13.525-15.925)	15.100 (13.575-16.125)	14.200 (12.500-14.550)	14.157 ± 1.690	14.471 ± 1.654	13.795 ±1.679	0.067	0.107
Thrombocytes (10^9/mL)	274.500 (230.500-318.500)	268.00 (223.000-300.750)	337.000 (286.500-341.000)	278.024 ± 69.361	273.455 ± 61.179	283.179±78.068	0.527	0.357

Data are presented as mean ± standard deviation, median (25–75th percentiles), or n (%) unless stated otherwise.
**P* value compares values of the COPD group vs the control group.
***P* value compares values of all 4 groups (COPD GOLD A through E and controls).
†Reflects statistical significance.
bpm: beats per minute; ALT: alanine transaminase; AST: aspartate transaminase; BSA: body surface area; GOLD: Global Initiative for Chronic Obstructive Lung Disease; K: potassium; Na: sodium; SBP: systolic blood pressure

Table 2: Comparison of Electrocardiographic and Pulmonary Function Test Findings According to the Presence and Severity of COPD

Parameter	COPD GOLD A	COPD GOLD B	COPD GOLD E	All Study Population	All COPD Patients	Control Group	*P value (COPD Group vs Controls)	**P value (COPD GOLD A Through E and Controls)
Subjects, n (%)	24 (28.2)	16 (18.8)	6 (7.1)	85 (100)	46 (54.1)	39 (45.9)		
Pulmonary Function Parameters								
FEV1 (L)	2.1850 (1.778-2.563)	1.930 (1.638-2.325)	1.155 (1.023-1.588)	2.460 ± 0.803	1.987 ± 1.498	3.017 ±0.629	<0.001†	<0.001†
% Predicted FEV1	67.000 (61.250-73.000)	57.000 (52.000-67.750)	45.000 (34.000-47.250)	76.020 ± 19.332	62.500 (52.000-68.425)	94.000 (89.000-100.000)	<0.001†	<0.001†
FVC (L)	2.915 (2.260-3.575)	2.910 (2.593-3.430)	1.775 (1.470-2.918)	3.188 ±0.898	2.827 ± 0.854	3.613 ±0.757	<0.001†	<0.001†
% Predicted FVC	78.000 (69.000-80.750)	74.000 (63.500-77.000)	57.000 (45.250-67.000)	81.635 ± 15.535	71.544 ± 11.189	92.000 (86.000-100000)	<0.001†	<0.001†
FEV1/FVC ratio (%)	73.750 (70.175-77.075)	67.700 (65.650-71.725)	64.600 (54.500-71.125)	76.554 ± 9.628	71.150 (66.100-74.650)	83.800 (80.900-87.100)	<0.001†	<0.001†
Electrocardiographic Parameters								
BBB‡, n (%)	8 (33.3)	2 (12.5)	1 (16.7)	12 (14.1)	11 (23.9)	1 (2.6)	0.005†	0.009†
RBBB‡	8 (33.3)	2 (12.5)	1 (16.7)	12 (14.1)	11 (23.9)	1 (2.6)		
LBBB‡	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)		

Data are presented as mean ± standard deviation, median (25–75th percentiles), or n (%) unless stated otherwise.
**P* value compares values of the COPD group vs the control group.
***P* value compares values of all 4 groups (COPD GOLD A through E and controls).
†Reflects statistically significant.
‡Reflects complete and incomplete bundle branch block morphology.
BBB: bundle branch blocks; GOLD: Global Initiative for Chronic Obstructive Lung Disease; FEV1: forced expiratory volume in 1 second; FVC: forced vital capacity; K: potassium; LBBB: left bundle branch block; RBBB: right bundle branch block

Table 3: Comparison of Conventional Echocardiographic Parameters According to the Presence and Severity of COPD

Parameter	GOLD A	GOLD B	GOLD E	All Study Population	All COPD Patients	Control Group	*P value (COPD Group vs Controls)	**P value (COPD GOLD A Through E and Controls)
Subjects, n (%)	24 (28.2)	16 (18.8)	6 (7.1)	85 (100)	46 (54.1)	39 (45.9)		
Conventional Echocardiographic Parameters								
Aortic root diameter (cm)	2.380 (2.170-2.598)	2.435 (2.178-2.555)	2.195 (2.143-2.283)	2.404± 0.269	2.365 ±0.255	2.450 ± 0.281	0.146	0.315
LAD (cm)	2.985 (2.653-3.248)	3.115 (2.720-3.478)	2.840 (2.645-3.223)	3.095 ±0.404	2.990 (2.710-3.320)	3.210 (3.000-3.350)	0.025†	0.008†
IVSd (cm)	1.020 (0.903-1.128)	0.940 (0.893-1.156)	1.015 (0.823-1.095)	1.001 ±0.223	0.950 (0.898-1.113)	1.010 (0.920-1.070)	0.717	0.774
LVPWd (cm)	0.920 (0.833-1.025)	0.875 (0.808-1.025)	0.905 (0.820-1.003)	0.918 ±0.104	0.880 (0.828-1.010)	0.900 (0.850-0.980)	0.947	0.954
LVIDd (cm)	4.095 (3.615-4.495)	4.220 (3.815-4.380)	3.975 (3.540-4.288)	4.212 ±0.415	4.130 (3.653-4.390)	4.340 (4.080-4.600)	0.007†	0.04†
LVIDs (cm)	2.805 (2.393-3.058)	2.580 (2.550-2.988)	2.475 (2.055-2.958)	2.646 ±0.371	2.665 (2.418-3.028)	2.570 (2.330-2.790)	0.190	0.374
LVEDV (ml)	54.800 (48.450-62.950)	58.050 (48.150-74.325)	58.450 (55.100-69.875)	57.413 ±15.101	57.398 ±14.518	57.431 ±15.953	0.992	0.430
LVESV (ml)	19.800 (17.150-24.500)	20.050 (14.625-31.100)	25.350 (21.825-28.600)	21.412 ±7.326	21.761 ±7.358	21.000±7.361	0.636	0.341
RAD (cm)	3.145 (2.815-3.408)	3.080 (2.845-3.368)	3.080 (2.780-3.240)	3.120 ±0.345	3.140 (2.890-3.363)	3.340 (3.200-3.460)	0.001†	0.01†
RVDd (cm)	3.025 (2.690-3.118)	2.890 (2.573-3.085)	2.835 (2.350-3.073)	2.931 ±0.331	2.899 ±0.347	2.969 ±0.311	0.336	0.475
PAD (cm)	1.800 (1.673-1.870)	1.855 (1.660-2.065)	1.875 (1.813-2.250)	1.806 ±0.240	1.845 ±0.238	1.760 ±0.237	0.102	0.131
TAPSE (cm)	2.240 (2.133-2.570)	2.280 (2.105-2.665)	2.350 (2.083-2.475)	2.435 ± 0.316	2.360 ± 0.283	2.523 ±0.334	0.017†	0.036†

LVEF (%)	62.800 (60.800-65.900)	67.500 (62.150-69.625)	61.100 (60.875-61.600)	64.333 ± 3.259	64.054±3.443	64.661±3.038	0.395	0.008†
E wave	0.630 (0.535-0.798)	0.740 (0.585-0.853)	0.785 (0.615-0.853)	0.718 ±0.184	0.711 ±0.202	0.727 ± 0.164	0.692	0.288
A wave	0.665 (0.495-0.778)	0.625 (0.558-0.738)	0.690 (0.630-0.935)	0.658 ±0.168	0.680 ±0.182	0.633 ± 0.148	0.205	0.396
Mitral E/A ratio (cm/s)	1.014 (0.746-1.355)	1.327 (0.778-1.385)	0.874 (0.782-1.354)	1.235 (0.779-1.400)	1.093 ±0.336	1.201 ± 0.337	0.142	0.304
Diastolic dysfunction							0.176	0.326
Grade I, n (%)	12 (50)	6 (37.5)	4 (66.7)	35 (41.2)	22 (47.8)	13 (33.3)		
Grade II, n (%)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)		
PHT, n (%)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)		
Heart valvular diseases§, n (%)								
Aortic valve disease	1 (4.2)	0 (0)	1(16.7)	3 (3.5)	2 (4.3)	1 (2.6)	0.657	0.288
Mitral valve disease	5 (20.8)	3 (18.8)	2 (333)	13 (15.3)	10 (21.7)	3 (7.7)	0.073	0.266
Tricuspid valve disease	5 (20.8)	5 (31.3)	3 (50.0)	21 (24.7)	13 (28.3)	8 (20.5)	0.409	0.393
Pulmonary valve disease	0 (0)	0 (0)	0 (0)	1 (1.2%)	0 (0)	1 (2.6)	0.275	0.755

Data are presented as mean ± standard deviation, median (25–75th percentiles), or n (%) unless stated otherwise.
**P* value reflects the comparison values of the COPD group vs the control group.
***P* value reflects the composition values of all 4 groups (COPD GOLD A through E and controls).
†Reflects statistical significance.
§Comprises minimal to mild degrees of heart valve diseases.
GOLD: Global Initiative for Chronic Obstructive Lung Disease; IVSd: interventricular septal end-diastolic thickness; LVEF: left ventricular ejection fraction; LVIDd: left ventricular internal end-diastolic diameter; LVIDs: left ventricular internal end-systole diameter; LVEDV: left ventricular biplane end-diastolic volume; LVESV: left ventricular biplane end-systolic volume; LVPWd: left ventricular posterior wall end-diastolic thickness; PAD: pulmonary artery diameter; PASP: pulmonary arterial systolic pressure; PHT: pulmonary hypertension; RAD: right atrial diameter, RVDd: right ventricular end-diastolic diameter; STE: speckle-tracking echocardiography; TAPSE: tricuspid annular plane systolic excursion

Table 4: Comparison of the Study Population as Speckle-Tracking-Based Echocardiographic Parameters According to the Presence and Severity of COPD

Parameter	COPD GOLD A	COPD GOLD B	COPD GOLD E	All Study Population	All COPD Patients	Control Group	*P value (COPD Group vs Controls)	**P value (COPD GOLD A Through E and Controls)
Subjects, n (%)	24 (28.2)	16 (18.8)	6 (7.1)	85 (100)	46 (54.1)	39 (45.9)		
STE-Based Evaluation of LVLS (%)								
AP2 LVLS	-21.300 (-24.900/-20.300)	-22.100 (-26.800/-19.200)	-19.500 (-20.425/-18.450)	-22.364 ±4.221	-22.121 ±4.122	-22.639 ±4.538	0.580	0.206
AP3 LVLS	-25.500 (-28.925/-21.250)	-21.250 (28.925/-18.700)	-19.800 (-23.175/-15.825)	-23.730 ± 5.265	-24.122 ±5.833	-23.269 ±4.538	0.460	0.056
AP4 LVLS	-21.800 (-24.475/-19.975)	-23.000 (-25.350/-19.550)	-20.500 (-24.100/-17.400)	-22.775 ±3,716	-22.280 ±3,379	-23,359 ± 4,046	0.184	0.550
GLS	-22.950 (-24.525/-21.225)	-22.250 (-25.775/-19.300)	-20.400 (-22.350/-16.800)	-22.867 ± 3.599	-22.663 ±3.721	-23.108 ±3.483	0.573	0.195
GTLSSD (ms)	21.800 (11.800-39.100)	19.650 (12.650-28.025)	20.750 (15.900-32.800)	26.807 ±21.187	19.700 (12.350-35.300)	22.000 (7.900-43.700)	0.921	0.992
STE-Based Evaluation of LV Circumferential Strain (%)								
Apical-CS	-31.600 (34.100/-28.700)	-28.000 (-39.900/-19.500)	-26.350 (-39.800/-20.950)	-29.847 ± 8.962	-30.514 ± 8.619	-29.095 ±9.390	0.475	0.398
Mid-CS	-23.900 (-29.600/-20.100)	-22.400 (-28.700/-17.900)	-21.450 (-22.400/-17.000)	-25.269± 6.275	-24.043 ± 5.944	-26.651 ±6.426	0.058	0.057
Basal-CS	-20.750 (-25.700/-19.975)	-19.550 (-23.775/-17.500)	-17.500 (-19.325/-16.200)	-22.435± 5.023	-21.200 ±3.888	-23.704 ±5.745	0.0026†	0.007†
GCS	-25.050 (-29.100/-21.150)	-22.450 (-29.025/-18.475)	-21.750 (-24.100/-18.850)	-24.180 ± 5.155	-24.324 ±5.066	-26.039 ±5.320	0.098	0.127
GTCSSD (ms)	28.450 (8.550-36.825)	23.700 (10.400-30.000)	29.100 (16.300-39.750)	28.900 (9.150-38.775)	25.500 ±16.561	31.800 (7.700-43.600)	0.389	0.754

Data are presented as *mean ± standard deviation, ¥median (25–75th percentiles), or n (%) unless stated otherwise.
**P* value reflects the comparison values of the COPD group vs the controls.

**P value reflects the comparison values of all 4 groups (COPD GOLD A through E and controls).
AP2: apical 2-chamber view; AP3: apical 3-chamber view; AP4: apical 4-chamber view; CS: circumferential strain; GCS: global circumferential strain; GLS: global longitudinal strain; GOLD: Global Initiative for Chronic Obstructive Lung Disease; GTCSSD: global time to peak circumferential strain standard deviation; GTLSSD: global time to peak longitudinal strain standard deviation; LV: left ventricular; LS: longitudinal strain; STE: speckle-tracking echocardiography.
†Statistically significant

DISCUSSION

The study performed conventional and STE-based echocardiography imaging to evaluate the extent to which COPD and HF mutually exert a negative impact. Although standard echocardiographic LV indices did not offer intercohortal differences, STE-based LV strain analysis presented regional-level subclinical LV systolic dysfunction in patients with COPD, compared to controls. Moreover, the study determined that the basal circumferential strain was impaired in COPD patients and correlated with the severity of COPD.

Contrary to the studies mentioned earlier, [18,19] in our study, the global or regional longitudinal strain did not relevantly vary for COPD patients (P=0.573). Although echo-graded diastolic dysfunction has been repeatedly determined in patients with COPD [19], this study found no association between COPD and LV diastolic dysfunction (P=0.176), either within COPD severity degrees (P=0.326). The exclusion of risk factors that may cause LV dysfunction from the study might have yielded reverse results. Similar to our results, another study reported no association between diastolic dysfunction and COPD. [18] Our study identified a rising prevalence of RBBB among COPD patients (P=0.005), that per se attenuates septal deformation properties without affecting LV diastolic performance, as assessed by standard echocardiography.

None of the study population had clinical evidence of cor pulmonale and pulmonary arterial pressure. However, as indicated by TAPSE levels, impaired RV systolic function was present in the COPD patients compared with controls. Thus, the subclinical RV dysfunction supports the early occurrence of RV impairment without evidence of overt pulmonary hypertension in COPD. Furthermore, these findings of RV dysfunction in patients with COPD complement some observations. [7,20]

In study populations in the literature, general cardiovascular stressors, such as arrhythmias, diabetes, hypertension, dyslipidemia, old age, valvular heart disease more than mild degrees, and renal failure, which COPD often accompanies, may cause a pseudo-association between COPD and LV dysfunction. In this study, patients and control participants were selected without comorbidities to minimize the effects of these external factors. In addition, none of the study population had clinical evidence of LV or RV dysfunction. Therefore, regional LV dysfunction difference was found even in early-stage COPD patients without comorbidities. In this context, our findings suggest a possible potential mechanism underlying the excess risk of HF in COPD.

In the study, regional LV dysfunction was related to the severity of airway obstruction and smoking packs/year of exposure. Further, lung function test parameters were predictive.

Limitations of the Study

Differences in cigarette exposure between patient and control groups are potentially confounding; hence, smoking packs/year was included in linear regression analysis. The restricted sample size in this study does not allow direct associations between COPD and cardiac functions to be inferred. Nevertheless, this study has shown

associations that should be explored further. Furthermore, we did not assess the functioning of other atria or ventricles via STE.

CONCLUSIONS

This study in clinically stable COPD patients without comorbidities and with a wide range of severity of airway disease provides new evidence that subclinical LV and RV dysfunction are often occult. LV systolic dysfunction was related to the severity of airway obstruction.

Acknowledgments
None.

Conflict of Interest
The authors declare that there is no conflict of interest.

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