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ECHOCARDIOGRAPHIC CHANGES OF THE LEFT VENTRICLE AND LEFT ATRIUM IN COPD

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Abstract. Introduction: *Cardiac disorders are common in patients with chronic obstructive pulmonary disease (COPD). They worsen shortness of breath and physical capacity and reduce the quality of life. Ultrasound assessment of cardiac function could contribute to assessing the severity of the disease. This study aimed to assess the prognostic significance of echocardiographic parameters on the rate of exacerbations and mortality.* ***Materials and methods:*** *This was a prospective study of patients with COPD without exacerbation in the previous 1 month. Patients over 40 years of age, current or former smokers with more than 10 pack-years of smoking, and postbronchodilator FEV1/FVC < 0.7 were included. All patients underwent two-dimensional transthoracic Doppler echocardiography at rest by an experienced cardiologist. Echocardiographic parameters were evaluated for prognostic significance on a composite endpoint of moderate and severe exacerbations and death for 1 year. Data from postbronchodilator spirometry, symptoms, quality of life, and demographic and clinical information were also collected.* ***Results:*** *A total of 96 patients were analyzed with a mean FEV1 of 55.8%. A total of 64 patients (67%) reached the composite endpoint. A significantly higher proportion of patients with deceleration time deviations (86.2 vs. 58.2%, p = 0.0055) and increased septal thickness (55.6 vs. 24.6%, p = 0.0099) reached the primary endpoint at one-year follow-up. Echocardiographic disorders showed a correlation with the quality of life, but not with lung function.* ***Conclusion:*** *Non-invasive assessment of cardiac function by echocardiography could be included in the complex assessment of disease severity in COPD patients.*

Key words: *COPD, echocardiography, predictors, left ventricle, left atrium, exacerbations*

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INTRODUCTION

Chronic obstructive pulmonary disease (COPD) is a leading cause of morbidity, mortality, and healthcare costs worldwide [1]. Cardiovascular diseases are the most common and important comorbidity in patients with COPD. Non-invasive assessment of cardiac function by echocardiography could contribute to the assessment of disease severity.

This study aims to assess the prognostic significance of echocardiographic parameters on a composite endpoint of moderate and severe exacerbations of COPD or death for one year. The correlation of echo-

cardiographic parameters with quality of life and severity of the disease was also analyzed.

MATERIALS AND METHODS

This was an observational, prospective study. The primary endpoint was a composite endpoint consisting of time to the first moderate or severe exacerbation or death.

Moderate exacerbation was defined as an acute worsening of respiratory symptoms requiring outpatient treatment with antibiotics and/or systemic steroids. When hospital treatment or emergency room care was required for more than 24 hours, the exacerbation was considered severe.

This study was approved by a local ethics committee. All participants continued the usual treatment regimen at the discretion of the attending physician.

Patients over 40 years, current or former smokers with more than 10 pack-years, and diagnosed with COPD by postbronchodilator FEV1/FVC ratio < 0.7 were included. Patients had to be in a stable condition for at least one month before inclusion. Exclusion criteria were the presence of other lung diseases (cystic fibrosis, severe bronchiectasis, carcinoma, or restrictive lung disease), systemic inflammatory disease, and lack of compliance with procedures (eg. completion of quality of life questionnaires). A patient was considered lost on follow-up if prospective follow-up data could not be obtained.

During the first visit, demographic characteristics (age and gender) and clinical characteristics of the disease were collected – postbronchodilator spirometry, and the number and type of exacerbations in the previous year. Shortness of breath was assessed with the modified Medical Research Council (mMRC) scale, and quality of life was assessed using the COPD Assessment Test (CAT).

All patients underwent two-dimensional transthoracic Doppler echocardiography at rest by an experienced cardiologist. A sector transducer with a frequency of 2-3.5 MHz in 2D and M-Mode modes was used. The function of the left ventricle was assessed using the following parameters:

- morphology – telediastolic diameter (TDD), telesystolic diameter (TSD), septal thickness, left ventricular posterior wall (LVPW) thickness, and volume and diameter of the left atrium;
- EF (ejection fraction) – the ejected volume from the end of the diastole at each contraction, calculated by the Simpson method:

EF = (EDV - ESV) / EDV x 100, normal value > 55%,

where EF is the ejection fraction, EDV is the end-diastolic volume and ESV is the end-systolic volume. Left ventricular ejection fraction below 50% is classified as heart failure (HF) with mildly reduced EF, and EF < 40% determines HF with reduced EF (HFrEF).

- FS (fractional shortening) – the percentage change in the size of the left ventricle for each contraction, calculated by the formula:

(LVEDD - LVESD / LVEDD) x 100,

where LVEDD is the left ventricular end-diastolic diameter and LVESD is the left ventricular end-systolic diameter. Values < 25% are classified as reduced FS.

- E/A – left ventricular diastolic filling, the ratio between the peak mitral flow rate of the early rapid filling wave (E) and the late filling wave peak rate caused by atrial contraction (A).

Patients were followed up for 12 months, and the number and type of exacerbations during the respective period were collected at 6 and 12 months with a structured questionnaire.

The selection of optimal cut-off points for the individual parameters was done using the cutpointr package (https://cran.r-project.org/web/packages/cutpointr/vignettes/cutpointr.html) to maximize the metric function *Youden's J (method = maximize_metric, metric = youden)*. The latter is calculated by the following formula:

J = sensitivity + specificity - 1

and is used in determining the ROC curve. The estimated cut-off value was used to divide the groups and perform subsequent analysis. The data were analyzed with RStudio v1.4.1106.

RESULTS

Population characteristics

A total of 96 patients with COPD were included. The mean age was 65.1 (standard deviation (SD): 8.1) years, the mean FEV1 was 55.8% (SD: 18.3%). Table 1 summarizes the characteristics of the patients included. No patients were lost during follow-up, and 3 patients (3/96, 3.1%) died during follow-up.

Echocardiographic parameters

Table 2 presents the echocardiographic parameters. 16.7% (16/96) had a reduced ejection fraction (< 55%) and 14.6% (8/96) of patients had a reduced fractional shortening (< 25%).

Table 1. Demographic and disease characteristics

Characteristic (± SD)	All patients (n = 96)
Age, mean, years	65.1 ± 8.1
Male, n (%)	60 (62.5%)
Active smokers, n (%)	33 (34.4%)
Pack-years, mean	28.5 ± 14.9
FEV1, %	55.8 ± 18.3
FVC, %	77.9 ± 22.5
CAT score	15.6 ± 9.2
mMRC score:	
0	11 (11.5%)
1	15 (15.6%)
2	28 (29.2%)
3	41 (42.7%)
4	1 (1%)
Moderate exacerbations in the previous year	
– mean (± SD)	0.73 ± 0.84
– median (IQR)	1 (0-1)
Severe exacerbations in the previous year	
– mean (± SD)	0.97 ± 0.87
– median (IQR)	1 (0-1)
Moderate exacerbations after 1 year	
– mean (± SD)	0.86 ± 0.90
– median (IQR)	1 (0-1)
Severe exacerbations after 1 year	
– mean (± SD)	0.45 ± 0.87
– median (IQR)	0 (0-1)

Abbreviations: SD – standard deviation; IQR – interquartile range

Table 2. Echocardiographic parameters

Characteristic	Value (± SD)
TDD	45.9 ± 6.2 mm
TSR	30.7 ± 5.8 mm
EF	60.9 ± 7%
FS	32.4 ± 4.9%
Septum	11.4 ± 1.4 mm
Left ventricular posterior wall thickness	11.3 ± 1.3 mm
Left atrium area	18.0 ± 4 mm^2
Left atrium size	35.2 ± 3.8 mm
E/A	0.80 ± 0.20
DT	218 ± 42 msec

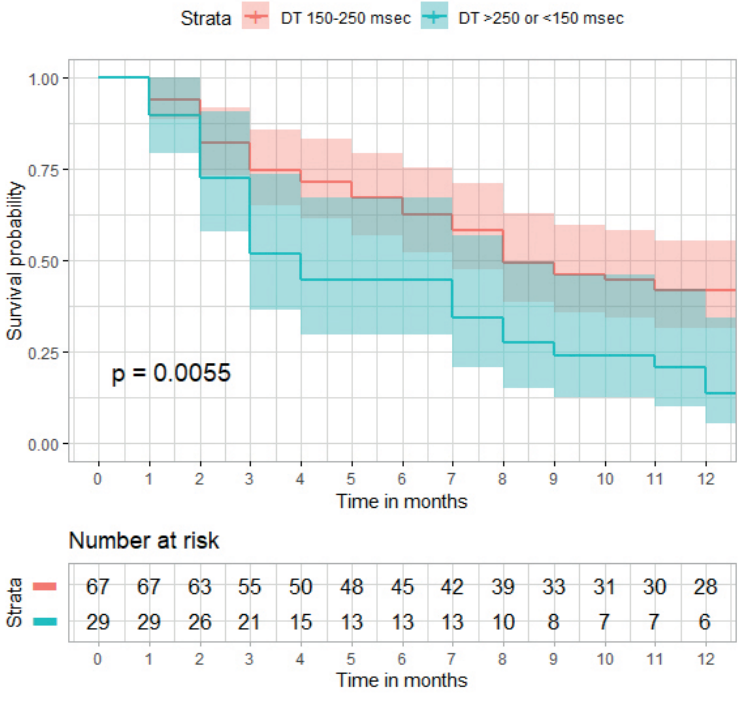
Abbr.: DT – deceleration time, E/A – left ventricular diastolic filling, TDD – telediastolic diameter, TSD – telesystolic diameter, EF – ejection fraction, FS – fractional shortening

Echocardiographic parameters and the primary endpoint

In the whole group, 64 patients (67%) reached the primary composite endpoint.

A significantly higher percentage of patients with abnormal DT (≥ 250 msec or < 150 msec) reached the primary endpoint (86.2% vs. 58.2, p = 0.0055) (Fig. 1).

Patients with lower FS (78.6 vs. 57.4% at cut-off 32%, p = 0.049) and larger left atrium (58.3 vs. 80.6% at cut-off 36 mm, p = 0.019) were more likely to reach the primary endpoint.



Abbr.: DT – deceleration time

Fig. 1. Survival curve for reaching the primary endpoint (time to exacerbation or death), stratified by deceleration time

Patients in the two groups did not differ regarding TDD (optimal cut-off 43.5 mm, p = 0.09), TSD (optimal cut-off 29 mm, p = 0.07), left atrial area, E/A ratio, and EF (all p > 0.2).

Patients with increased septal thickness were significantly more likely to reach the primary endpoint (55.6 vs. 24.6% at cut-off 10.5 mm, p = 0.0099) (Fig. 2). A similar result was observed for LVPW (55.6 against 24.6% at cut-off 10.5 mm, p = 0.019) (Fig. 3).

Echocardiographic parameters and exacerbations

Patients with normal DT (150-250 msec) had significantly less exacerbations (1.1 vs. 1.8, p = 0.01). This was due to significantly less severe exacerbations (0.29 vs. 0.85, p = 0.016), while the frequency

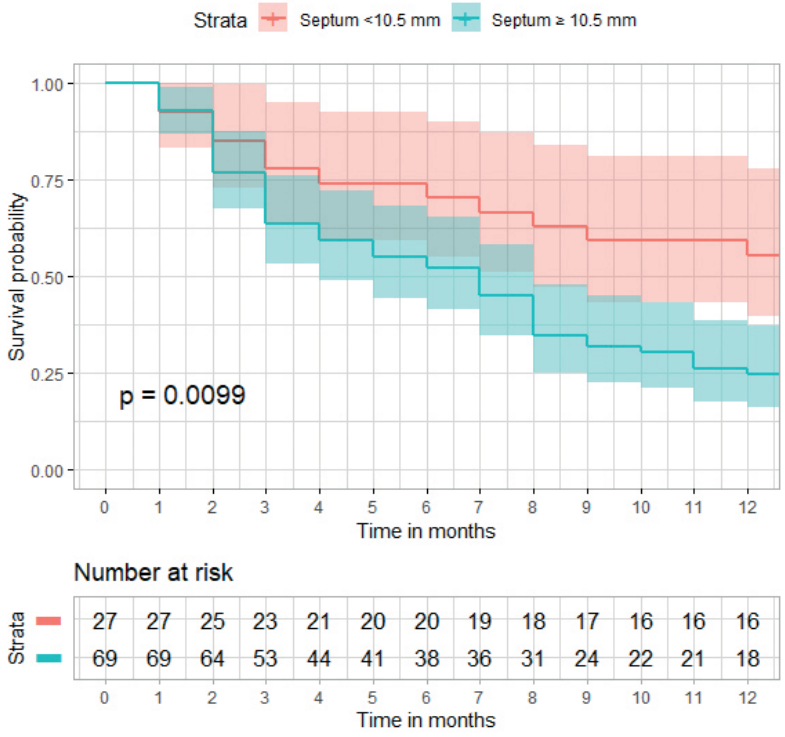
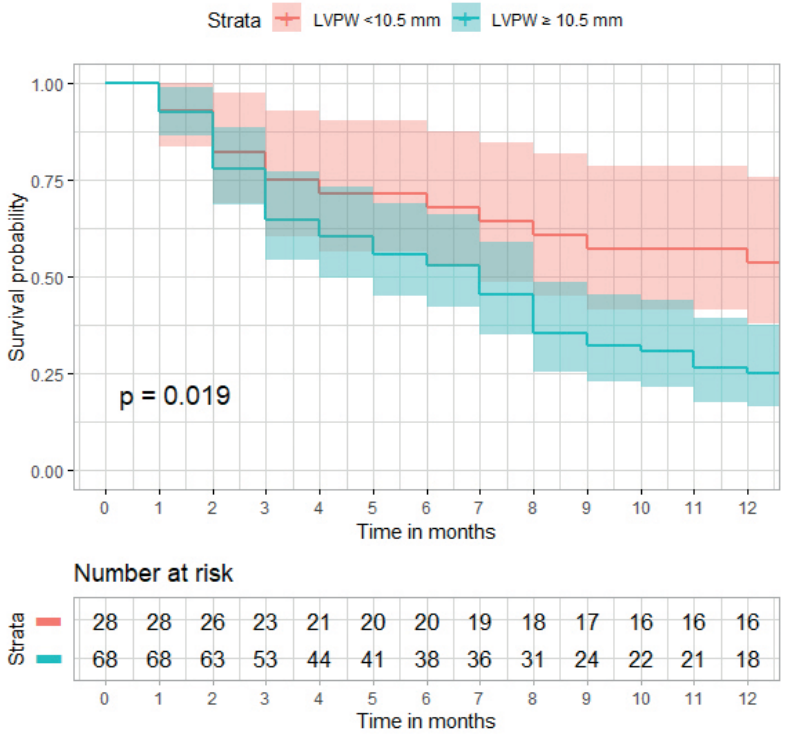


Fig. 2. Survival curve for reaching the primary endpoint (time to exacerbation or death), stratified by the septal thickness



Abbr.: LVPW – left ventricular posterior wall

Fig. 3. Survival curve for reaching the primary endpoint (time to exacerbation or death), stratified by LVPW thickness

of moderate exacerbations did not differ (0.8 vs. 1.0, p = 0.32).

Left atrial size was not a significant predictor of the frequency of total exacerbations or moderate and severe exacerbations. Patients with FS ≥ 32% had a significantly lower number of exacerbations (1.04 vs. 1.61, p = 0.025).

Septum thickness was not a predictor for total or severe exacerbations but was a predictor for moderate exacerbations (0.52 vs. 1.0 at cut-off 10.5 mm, p = 0.01). The results for LVPW were similar (moderate exacerbations: 0.57 vs. 0.98 at a cut-off 10.5 mm, p = 0.036).

Echocardiographic parameters and quality of life

The mean CAT score was 15.6 points and the mMRC scores of 0, 1, 2, 3 and 4 were having 11 (11.5%), 15 (15.6%), 28 (29.2%), 41 (42.7%) and 1 (1%) patients, respectively (Table 1).

Left atrial size < 36 mm or normal DT was associated with a better quality of life, as demonstrated by a lower CAT score (13.9 vs. 18.5, p = 0.019, and 14.3 vs. 18.6, p = 0.048, respectively). Similarly, patients with a septum ≥ 10.5 mm had impaired quality of life (16.8 vs. 12.6 CAT points, p = 0.04). There is a tendency for lower quality of life in patients with FS < 32% (14 vs. 17.8, p = 0.0503).

Echocardiographic parameters and lung function

Although FEV1 was numerically higher in the group with normal DT, the results did not reach statistical significance (57.8 vs. 51.0%, p = 0.099). There is no difference in lung function regarding the left atrial size, FS, septal thickness, or LVPW thickness.

DISCUSSION

COPD is a chronic respiratory disease characterized by systemic inflammation [2], which increases the risk of exacerbations and more or more severe comorbidities [2]. Exacerbations play an important role in the natural course of COPD, being one of the leading causes of death [3].

Cardiac manifestations of COPD are numerous. Significant structural changes in the pulmonary circulation occur in patients with COPD. Cardiac disorders in COPD could be due to chronic hypoxemia leading to impaired myocardial relaxation, hyperinflation of the lungs, leading to increased rigidity of the parietal pleura and thus the wall of the cardiac fossa, which leads to additional strain on the chamber, and due to ventricular interdependence. This impairs left ventricular function in patients with COPD [4, 5].

This manuscript shows that a significantly higher proportion of patients with abnormal deceleration time, increased thickness of the septum and LVPW reach the primary endpoint (exacerbation or death) at one-year follow-up. DT correlates with the frequency of exacerbations (particularly severe exacerbations), and the thickness of the septum and LVPW correlates with moderate exacerbations. Left atrial size, septum thickness, and DT correlate with the quality of life. Interestingly, none of the studied parameters showed a relationship with lung function.

The prevalence of left ventricular systolic dysfunction in patients with COPD is 4–32% [6-9], which was in concordance with our findings (16.7%). One study showed a 74% incidence of left ventricular diastolic dysfunction in patients with COPD, with a higher prevalence in patients with more impaired lung function [10].

Regarding airway obstruction, lower FEV1 correlates with lower E (dt), suggesting a relationship between airway resistance and left ventricular diastolic pressure and relaxation. In addition, the positive intrathoracic pressure during expiration, combined with prolonged expiratory time, could maintain increased intrathoracic pressure for most of the respiratory cycle, thus reducing venous return and disrupting ventricular filling and cardiac output [11].

CONCLUSION

Cardiac disorders are common in patients with COPD. Some easily measurable echocardiographic parameters such as deceleration time and thickness of the septum and left ventricular posterior wall show a significant correlation with the likelihood of exacerbation or death at one-year follow-up. Non-invasive assessment of cardiac function by echocardiography could be included in the comprehensive assessment of disease severity.

Disclosure Summary: *The authors have nothing to disclose.*

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