

Research Article

Atrial Conduction Times and Longitudinal Strain of Patients with Chronic Obstructive Pulmonary Disease

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Abstract

Objectives: The study aimed to compare atrial electromechanical delay (AEMD), apical 4-chamber longitudinal strain (4C-LS), echocardiographic changes and blood parameters in patients with COPD and control group.

Methods: This prospective study was conducted in February and July 2018. The study included 90 (43 females, 47 males) patients with acute COPD exacerbation (Group 1), 92 (19 females, 73 males) stable COPD out-patients (Group 2) and 79 (43 females, 36 males) control group patients (Group 3). Demographic features, atrial conduction times, longitudinal strains, systolic-diastolic functions of right-left heart and blood parameters were compared. Statistical analysis was carried out using SPSS software.

Results: Basal anterolateral, mid anterolateral, apicolateral, apex, apical septal, mid inferoseptal, basal inferoseptal and 4C-LS were lower in Group 1. RV basal and mid diameters, Amax, Aa, TRV, SPAP, Emax mitral, Ea mitral, Ea/Aa mitral, Aa septum and heart rate were significantly higher and RV vertical diameter, TAPSE, Emax/Amax, Ea/Aa, end-diastolic diameter, LVEF, Ea septum, Ea/Aa septum were significantly lower in Group 1. Lateral/mitral AEMD, lateral/tricuspid AEMD and septal AEMD were higher in Group 1 compared to other groups ($p < 0.001$).

Conclusion: Right-left ventricular systolic-diastolic functions were impaired in patients with acute COPD exacerbation. In these patients, longitudinal strain rates were lower and AEMD was prolonged.

Keywords: Atrial electromechanical delay; chronic obstructive pulmonary disease; strain

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Chronic obstructive pulmonary disease (COPD) is characterized by increased chronic and progressive inflammation.^[1, 2] COPD effects mainly lungs but it has some important extra pulmonary effects such as cardiovascular abnormalities that contribute to disease severity.^[2, 3] Cardiovascular disorders are the leading causes of mortality in patients with mild-to-moderate COPD and many of these patients remain undiagnosed.^[4] The development, evaluation and prevalence of cardiovascular comorbidities in COPD patients have not been totally clarified but clinically

important manifestations such as myocardial infarction, heart failure secondary to COPD and arrhythmias are the most common conditions.^[4, 5] COPD also affects right ventricle, pulmonary blood vessels, left ventricle and causes pulmonary hypertension, cor pulmonale, and right-left ventricle dysfunction.^[6]

Atrial fibrillation (AF) is the most commonly encountered arrhythmia in clinical practice and is related to increased mortality and morbidity.^[7] COPD is independently associated with AF but the pathophysiological mechanism is not

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completely clarified.^[7] Increased atrial automaticity, trigger activity, micro re-entry, and abnormal atrial tissue are responsible mechanism of AF.^[8] Atrial electromechanical delay (AEMD) is the time interval between the beginning of P wave on surface electrocardiography and beginning of the late diastolic wave (Am-wave) on Tissue Doppler Imaging (TDI).^[9] The structural changes of atrial tissue causes delay between the electrical stimulation and mechanical contraction.^[9] Atrial tissue changes can cause prolongation P wave on surface electrocardiogram (ECG).^[10] Prolongation of P wave can be seen in patients undergoing coronary artery bypass surgery, patients with hypertrophic cardiomyopathy, right atrial dilatation, atrial septal defect, hypertension and COPD due to affected atrial tissue.^[10]

Two-dimensional speckle tracking echocardiography (2D-STE) is a strain measurement method to obtain the size of regional myocardial deformation.^[11,12] Myocardial deformations can be obtained by this easily applied method in the longitudinal, circumferential and radial pointing.^[11,12]

The aim of this study was to compare AEMD, apical 4-chamber longitudinal strain (4C-LS), echocardiographic changes and blood parameters in patients with COPD and control group.

Methods

Design and Assessment

This prospective study was conducted with the approval of a university hospital ethics committee, Causacian University, Kars, Turkey, between February 2018 and July 2018. The study included 90 (43 females, 47 males) patients with acute COPD exacerbation who admitted to emergency room, 92 (19 females, 73 males) stable COPD out-patients who admitted to Respiratory Medicine Unit, stages I-IV, for both groups and 79 (43 females, 36 males) control group patients. Acute COPD exacerbation group was named as Group 1, stable COPD out-patients were Group 2 and control group patients were Group 3. Group 2 patients were stable with no acute exacerbation of disease for at least one month prior to admission and they were under regular treatment. Group 3 patients were admitted to the Chest Diseases Polyclinic for any reason, and were not diagnosed any disease, and they don't have prior disease history or medication. The exclusion criteria were as follows: patients with no previous COPD diagnosis (except for Group 3), patients with valvular heart disease, wall-motion abnormality, uncontrolled hypertension, insulin dependent diabetes mellitus, hypo-hyperthyroidism, anemia, acid-base disorders, electrolyte disorders, renal impairment, lipid abnormalities, coronary artery disease, acute coronary syndrome, heart failure, structural heart diseases, atrioventricular conduction abnormalities, ejection fraction <50%,

pulmonary embolism, pneumonia, malignancy, systemic inflammatory response syndrome, intubated patients after admission and patients using two or more oral antidiabetic drugs. The patients who had history of atrial fibrillation and prior use of antiarrhythmic drugs were excluded. The diagnosis of acute COPD exacerbation and stable COPD were in accordance with the criteria established by the European Respiratory Society and American Thoracic Society.^[13, 14] The following parameters of all patients were evaluated: age, gender, smoking status (smoker, ex-smoker, never smoker), body mass index (BMI), blood glucose, electrolytes, liver and renal function tests, complete blood count, blood gas analysis, pulmonary function tests and transthoracic echocardiography. Forced expiratory volume in the first second (FEV1) and forced vital capacity (FVC) were measured at baseline using a spirometer (Spirolab III-MIR, Italy). Echocardiography was performed in the first 24 hours for Group 1, in the first 6 hours for Group 2 and 3. All patients were informed about the study. Verbal consent was obtained for all procedures and then the patient's signature was accepted.

Blood Samples

Firstly, an alcohol swab was used to clean for skin and a band was used to tie for arm of patients. All blood samples were drawn from the vein in the forearm and collected into 2 mL Lavender (EDTA) top tube + 4 mL Yellow (Acid Citrate Dextrose) top tube. The samples were analysed with Pentra DF Nexus, Horiba Medical, Japan with Automated Cell Counter Methodology and Cobas C 702 Module, Roche, Switzerland. The complete blood count samples were stabilized optimally when run within in 4 hours of collection, stable for 24 hours at room temperature, and stable for 36 hours at 2–8 degrees C. The yellow top tube was centrifuged for 8-10 minutes at 3500-4000 revolution per minute (rpm) and serum was separated. The serum was stable for 8 hours at 2-8 degrees C.

Echocardiography

Transthoracic echocardiography (Epiq 7; Philips) was evaluated by a practitioner in a standard protocol in all patients. A 2.5 MHz probe was used for the Doppler measurements and 2.5-3.5 MHz probe for tissue Doppler measurements. Patients were monitored using electrocardiographic leads and were placed in the left lateral decubitus position. Echocardiographic images were obtained from the parasternal views (long axis, short axis), the apical four-chamber view and, the subcostal view. Echocardiographic measurements were performed at the end of expiration according to the recommendations of the American Society of Echocardiography/ European Association of Echocardiography.

graphy.^[15] 1) Diameters of right ventricle (RV), measured in apical view. 2) Left ventricle (LV) diameter and wall thickness were measured in the parasternal view. 3) Left atrial diameter, measured in the parasternal view. 4) Aortic root diameters, measured at the sinus of Valsalva. 5) LV ejection fraction (LVEF), measured in apical 4-chamber view by modified Simpson method. 6) Right and left ventricle functions were evaluated as follows: a) maximal peak velocity of early diastolic flow (E_{max}), maximal peak velocity of atrial contraction (A_{max}), and ratio of these (E_{max}/A_{max}), measured over the mitral and tricuspid valves; b) Tissue Doppler imaging, measured in the mitral and tricuspid lateral annulus at early diastole (E_a), atrium systole (A_a) and ratio of these (E_a/A_a); c) The ratio of E_{max}/E_a. 7) Aortic, tricuspid, mitral and pulmonary valvular evaluation. 8) Tricuspid regurgitant velocity (TRV) recorded by continuous wave Doppler.

AEMD was calculated from colored-TDI recordings. AEMD was determined as the time interval between the beginning of echocardiographic P wave to the initial of Am-wave (late diastolic wave) in TDI recordings. AEMD was measured from lateral/tricuspid, lateral/mitral and septal anulus from apical 4-chamber views.

The echocardiographic examinations, and standard 2D measurements for strain images were acquired according to American Society of Echocardiography recommendations.^[15] The images were digitally stored, and measurements were performed by same practitioner. Images were obtained at a frame rate of 50 to 70 per second, and digital loops were saved onto optical disc for off-line analysis. The cardiac cycle with the best image quality and without any

artefacts was selected for reporting results. Two and three-chambers images were not used due to intense artefacts. Longitudinal strain images were obtained apical 4-chamber views. The practitioner identified three points on each view (two borders of the mitral annulus and the apex). Speckles were tracked frame by-frame throughout the LV wall during the cardiac cycle and basal, mid, and apical regions of interest were created.

Statistical Analysis

All statistical calculations were performed with SPSS 23.0 (SPSS for Windows, Chicago, IL, SA). All continuous variables were expressed as mean±standard deviation; categorical variables were defined as percentages (%). The categorical parameters were compared with Chi-Square test and Fisher's exact test. The normal distribution was determined by histogram and Kolmogorov-Smirnov test. Mean values of continuous variables were compared between the groups using Mann-Whitney U test. All tests were applied as two tailed; the statistical significance level was p<0.05.

Results

Clinical and spirometric features

Clinical and spirometric characteristics of the study population are presented in Table 1. The mean age of all patients was 65.6±8.7 and the mean age of the patients in Group 1 was significantly higher than the others (p=0.005, p<0.001). 40.2% (n=105) of all the patients were female and 59.8% (n=156) were male. FEV1 and FVC were significantly lower in Group 1 patients compared to other groups (p<0.001).

Table 1. Clinical and spirometric characteristics of the groups

	Total	Patients groups			p			
		Group 1	Group 2	Group 3	Group 1 & 2	Group 1 & 3	Group 2 & 3	
		Mean±SD/n (%)						
Age	65.6±8.7	68.9±9	65.1±9.4	62.4±5.8	0.005	<0.001	0.058	
Gender								
Male	156 (59.8)	47 (52.2)	73 (79.3)	36 (45.6)				
Female	105 (40.2)	43 (47.8)	19 (20.7)	43 (54.4)				
Smoking								
Smoker	72 (27.6)	11 (12.2)	36 (39.1)	25 (31.6)				
Ex-smoker	93 (35.6)	40 (44.4)	39 (42.4)	14 (17.7)				
Never smoker	96 (36.8)	39 (43.3)	17 (18.5)	40 (50.6)				
BMI & Spirometry								
BMI	27.64±5.92	27.58±7.91	27.44±5.16	27.93±3.77	0.410	0.962	0.143	
FEV1	56.1±22.3	34.9±12	56.8±15.8	79.3±11.7	<0.001	<0.001	<0.001	
FVC	54.5±20.1	35.4±12.9	55.3±12.6	75.3±10.4	<0.001	<0.001	<0.001	

The continuous variables are expressed as mean±standard deviation; BMI: body mass index; FEV1: forced expiratory volume in the first second; FVC: forced vital capacity; Mann-Whitney-U test, Chi-Square test.

Biochemical blood parameters such as glucose, liver and renal function tests, total protein and C-reactive protein/albumin ratio (CAR) and electrolytes of the study population are presented in Table 2. Glucose, urea, creatinine, AST, potassium were higher in Group 1. CRP, CAR were significantly

higher and albumin was significantly lower in Group 1 compared to Group 2 and 3.

Complete blood counts of the study population are presented in Table 3. Hemoglobine, hematocrit, white blood cell (WBC), platelets, neutrophile, neutrophile percent,

Table 2. Biochemical blood parameters of the groups

	Total	Patient groups			p		
		Group 1	Group 2	Group 3	Groups 1 & 2	Group 1 & 3	Group 2 & 3
Mean±SD							
Blood parameters							
Glucose, mg/dL	102.9±25.4	111±34.6	100.5±21.1	96.3±11.3	0.016	0.003	0.784
Urea, mg/dL	37.5±14.3	42.2±16.3	37.4±14.3	32±8.7	0.015	<0.001	0.013
Creatinine, mg/dL	0.86±0.38	0.97±0.55	0.87±0.21	0.73±0.2	0.508	<0.001	<0.001
HDL, mg/dL	49.3±13.2	50±15.6	48.4±12	49.6±11.7	0.601	0.982	0.745
CRP, mg/L	1.91±4.91	4.33±7.7	0.84±1.03	0.36±0.43	<0.001	<0.001	<0.001
Albumin, g/L	4.36±0.42	4.2±0.35	4.36±0.3	4.54±0.54	0.003	<0.001	<0.001
CAR	0.46±1.28	1.05±2.06	0.2±0.25	0.09±0.15	<0.001	<0.001	<0.001
AST, u/L	22.3±10.4	27.3±13.3	19.6±7.1	19.8±7.2	<0.001	<0.001	0.929
ALT, u/L	19.4±11.4	21.3±13.1	17.7±9.1	19.3±11.5	0.148	0.638	0.254
Calcium, mg/dL	9±0.55	8.92±0.53	9.27±0.66	9.3±0.3	0.094	0.023	0.669
Sodium, mmol/L	139.9±2.5	139±2.8	140.2±2.1	140.4±2.3	0.005	<0.001	0.243
Potassium, mmol/L	4.57±0.47	4.76±0.57	4.53±0.41	4.4±0.33	0.003	<0.001	0.012
Protein, g/L	7.06±0.67	6.93±0.94	6.94±0.47	7.34±0.39	0.857	<0.001	<0.001

The continuous variables are expressed as mean±standard deviation; HDL: high density lipoprotein; CRP: C-reactive protein; CAR: C-reactive protein / albumin ratio; AST: aspartate transaminase; ALT: alanine aminotransferase. Mann-Whitney-U test, Chi-Square test.

Table 3. Complete blood count parameters of the groups

	Total	Patient groups			p		
		Group 1	Group 2	Group 3	Group 1 & 2	Group 1 & 3	Group 2 & 3
Mean±SD							
Complete blood count							
Hemoglobine, g/dL	15.6±1.97	15.9±2.09	15.99±2.02	14.79±1.48	0.969	<0.001	<0.001
Hematocrit, %	46.9±6	47.7±7.2	47.8±5.7	44.8±4.1	0.810	<0.001	<0.001
WBC, 10 ³ /uL	8.12±2.66	8.83±3.25	8.1±2.41	7.31±1.9	0.242	0.001	0.013
MPV, fL	8.73±0.83	8.76±0.8	8.64±0.84	8.81±0.84	0.452	0.520	0.210
Platelet, 10 ³ /uL	244.3±72.8	229.2±69	239.8±65.6	267.1±80.1	0.296	0.001	0.022
Lymphocyte, 10 ³ /uL	2.24±1.89	1.83±1.28	2.58±2.83	2.31±0.62	<0.001	<0.001	0.331
Lymphocyte, %	26.4±9.6	19.9±9.4	27.8±8.3	32.1±6.5	<0.001	<0.001	<0.001
PLR	136.15±77.51	162.33±104.96	121.23±55.6	123.54±50.92	0.008	0.026	0.568
Neutrophile, 10 ³ /uL	5.17±2.25	6.21±2.89	4.93±1.66	4.25±1.44	0.004	<0.001	0.005
Neutrophile, %	62.5±10.9	68.2±12.3	61±9.4	57.6±7.5	<0.001	<0.001	0.013
NLR	2.99±2.23	4.34±2.91	2.57±1.58	1.93±0.76	<0.001	<0.001	0.003
Eosinophile, 10 ³ /uL	0.19±0.16	0.16±0.13	0.21±0.13	0.19±0.2	0.003	0.196	0.065
Eosinophile, %	2.36±1.81	1.93±1.46	2.63±1.67	2.54±2.21	<0.001	0.001	0.430
RDW, %	15.7±2.3	16.33±2.77	15.54±2.05	15.18±1.8	0.016	0.001	0.307
PCT, %	0.21±0.06	0.2±0.06	0.21±0.05	0.24±0.07	0.495	<0.001	0.001

The continuous variables are expressed as mean±standard deviation; WBC: white blood cell; MPV: mean platelet volume; PLR: platelet-to-lymphocyte ratio; NLR: neutrophile-to-lymphocyte ratio; RDW: red cell distribution width; PCT: plateletcrit. Mann-Whitney-U test, Chi-square test.

neutrophile-to-lymphocyte ratio (NLR) were lower and plateletcrit (PCT) was higher in Group 3. Platelet-to-lymphocyte ratio (PLR), red cell distribution width (RDW) were higher and eosinophile, eosinophile percent were lower in Group 1.

Blood gas analysis of the study population are presented in Table 4. $p\text{CO}_2$ and HCO_3 were higher and $p\text{O}_2$ was lower in Group 1. Lactate was lower and anion gap was higher in Group 3.

Strain Echocardiography Evaluation

Two-dimensional speckle tracking (2D-ST) echocardiography findings of the study population are presented in Table 5. Basal anterolateral, mid anterolateral, apicolateral, apex, apical septal, mid inferoseptal, basal inferoseptal and 4C-LS were decreased in Group 1 compared to Group 3. Basal anterolateral, mid anterolateral, apicolateral, apex, apical septal, 4C-LS were decreased in Group 2 compared to Group 3. There was not significantly difference between Group 1 and 2.

Evaluation of Systolic-Diastolic Functions of Right-Left Heart

Echocardiographic findings of right-left heart and septum, and atrial conduction times of the study population are presented in Table 6. RV basal and mid diameters, Amax, Aa, TRV and SPAP were significantly higher and RV vertical diameter, TAPSE, Emax/Amax, Ea/Aa were significantly lower in Group 1 compared to other groups. Ea was lower in Group 2.

End diastolic diameter and LVEF were lower in Group 1. Interventricular septum and posterior wall thickness were lower in Group 3. Emax mitral, Ea (TD lateral mitral), Ea/Aa mitral were higher in Group 3. Amax mitral, Emax/Amax mitral, Aa (TD lateral mitral) were higher in Group 1. Ea septum, Ea/Aa septum were lower and Aa septum, heart rate were higher in Group 1.

Prolongation of lateral/mitral, lateral/tricuspid and septal AEMD were differed significantly between three groups

Table 4. Blood gas analysis of the groups

	Total	Patient groups			p		
		Group 1	Group 2	Group 3	Group 1 & 2	Group 1 & 3	Group 2 & 3
Mean±SD							
Blood gas analysis							
pH	7.42±0.03	7.42±0.04	7.42±0.03	7.43±0.03	0.289	0.679	0.065
$p\text{CO}_2$, mmHg	38.3±5.8	41.1±7.7	37.9±4	35.6±3	0.009	<0.001	<0.001
PO_2 , mmHg	57.3±10.3	48.6±8.7	58±6.6	66.6±6.2	<0.001	<0.001	<0.001
Lactate, mmol/L	1.19±0.56	1.37±0.72	1.19±0.42	0.99±0.42	0.212	<0.001	0.001
HCO_3 , mmol/L	24.9±2.7	26.1±3.6	24.5±1.6	24±1.8	<0.001	<0.001	0.062
Anion gap, mmol/L	12.9±1.93	12.57±2.33	12.7±1.7	13.52±1.47	0.405	0.001	0.001

The continuous variables are expressed as mean±standard deviation; pH: power of hydrogen; $p\text{CO}_2$: partial carbon dioxide pressure; $p\text{O}_2$: partial oxygen pressure; HCO_3 : bicarbonate. Mann-Whitney-U test, Chi-square test.

Table 5. 2D-ST echocardiography findings of the study population

	Total	Patient groups			p		
		Group 1	Group 2	Group 3	Group 1 & 2	Group 1 & 3	Group 2 & 3
Mean±SD							
Longitudinal Strain							
Basal Anterolateral	-18.59±4.53	-17.41±4.94	-18.09±4.53	-20.53±3.32	0.321	<0.001	<0.001
Mid Anterolateral	-18.96±4.85	-17.63±5.26	-18.73±5.11	-20.75±3.33	0.253	<0.001	0.002
Apicolateral	-19.95±4.39	-18.73±4.56	-19.66±4.77	-21.68±3.04	0.187	<0.001	0.001
Apex	-23.39±4.55	-22.11±4.91	-23.1±4.64	-25.2±3.3	0.256	<0.001	0.001
Apical septal	-26.88±5.56	-25.59±6.14	-26.61±5.5	-28.66±4.4	0.391	0.001	0.005
Mid inferoseptal	-15.52±4.4	-14.53±4.54	-15.48±4.67	-16.7±3.62	0.093	0.001	0.060
Basal inferoseptal	-14.39±3.56	-13.54±4.04	-14.4±3.5	-15.35±2.76	0.130	0.001	0.062
4C-LS	-19.44±3.61	-18.18±3.96	-19.21±3.6	-21.13±2.38	0.111	<0.001	<0.001

The continuous variables are expressed as mean±standard deviation; 4C-LS: four-chamber longitudinal strain. Mann-Whitney-U test. Chi-Square test.

Table 6. Echocardiographic findings of right-left heart and septum, and atrial conduction times of the study population

	Total	Patient groups			p		
		Group 1	Group 2	Group 3	Group 1 & 2	Group 1 & 3	Group 2 & 3
		Mean±SD					
Right Heart, RV Diameters (mm)							
Basal	34.6±5.4	37.1±5.6	35±5.1	31.3±3.3	0.001	<0.001	<0.001
Mid	24.4±5.4	28.1±5.6	23.9±3.8	20.6±3.9	<0.001	<0.001	<0.001
Vertical	49.6±6.5	47.4±7.2	49.1±6.1	52.6±4.7	0.030	<0.001	<0.001
TAPSE (mm)	24±4.3	20.9±3.8	23.9±3.4	27.6±2.6	<0.001	<0.001	<0.001
RV Functions, Diastolic Function							
Emax tricuspid (cm/s)	51.1±12.3	52.2±15.1	48±9.9	53.3±10.7	0.171	0.089	0.001
Amax tricuspid (cm/s)	58.9±16.5	70.2±18.3	54.3±12.7	51.3±10.4	<0.001	<0.001	0.154
Emax/Amax tricuspid	0.91±0.28	0.76±0.22	0.93±0.27	1.07±0.27	<0.001	<0.001	<0.001
Ea (TD tricuspid) (cm/s)	8.61±2.51	8.78±2.69	7.92±2.32	9.23±2.34	0.018	0.284	<0.001
Aa (TD tricuspid) (cm/s)	16.31±4.45	18.82±5.02	15.35±3.25	14.58±3.68	<0.001	<0.001	0.194
Ea/Aa tricuspid	0.56±0.23	0.5±0.23	0.53±0.16	0.68±0.25	0.022	<0.001	<0.001
Emax/Ea tricuspid	6.34±2.37	6.45±3.05	6.5±2.13	6.04±1.63	0.173	0.747	0.299
Assessment of pulmonary hypertension							
TRV (m/s)	2.694±0.482	3.049±0.378	2.723±0.38	2.256±0.318	<0.001	<0.001	<0.001
SPAP (mmHg)	29.7±10.3	37.4±8.9	29.9±8.1	20.8±5.7	<0.001	<0.001	<0.001
SM tricuspid	12.5±2.6	12.8±3	12±2.6	12.8±1.6	0.068	0.877	0.018
Pulmonary velocity	109.9±13.4	109.3±17.8	108.7±10	111.9±10.8	0.385	0.037	0.071
Left Heart							
LV Diameters (parasternal long axis)							
End-diastolic diameter (mm)	45.8±3.9	44.6±3.9	46.2±4	46.7±3.5	0.003	<0.001	0.237
End-systolic diameter (mm)	28±4.8	27.9±4	28.4±3.9	27.8±6.5	0.300	0.437	0.087
LV wall thickness							
Interventricular septum (mm)	11.4±1.3	11.7±1.4	11.6±1.3	10.8±1.2	0.722	<0.001	<0.001
Posterior Wall (mm)	10.2±1.2	10.4±1.3	10.3±0.9	9.8±1.1	0.791	0.006	0.002
LVEF, %	68.7±6.7	66.1±5.5	68.7±7.7	71.7±5.2	0.003	<0.001	0.010
Diastolic functions							
Emax mitral (cm/s)	66.9±16.4	65.4±18.2	63.9±15.4	72±14.1	0.656	0.003	<0.001
Amax mitral (cm/s)	86.7±28.2	97.9±37.8	85.5±18.9	75.1±17.8	0.002	<0.001	<0.001
Emax/Amax mitral	0.85±0.76	0.7±0.2	0.76±0.18	1.12±1.31	0.009	<0.001	<0.001
Ea (TD lateral mitral) (cm/s)	9.33±2.77	8.64±2.32	8.65±2.3	10.9±3.11	0.938	<0.001	<0.001
Aa (TD lateral mitral) (cm/s)	12.33±3.06	13.92±3.21	11.8±2.69	11.13±2.51	<0.001	<0.001	0.111
Ea/Aa mitral	0.81±0.37	0.65±0.22	0.77±0.29	1.05±0.46	0.001	<0.001	<0.001
Emax/Ea mitral	7.65±2.56	7.91±2.37	7.9±2.89	7.07±2.3	0.502	0.006	0.056
Septum							
Ea septum (cm/s)	6.75±2.03	6.26±1.76	6.44±1.67	7.66±2.39	0.397	<0.001	0.001
Aa septum (cm/s)	11.2±2.46	12.1±2.64	10.73±2.01	10.74±2.49	<0.001	0.001	0.947
Ea/Aa septum	0.63±0.24	0.53±0.16	0.61±0.17	0.75±0.32	0.001	<0.001	0.014
SM mitral	8.97±6.39	9.89±10.54	8.38±2.02	8.59±1.75	0.102	0.433	0.430
SM septal	7.48±1.56	7.45±1.74	7.38±1.53	7.64±1.36	0.739	0.273	0.146
Heart rate, beats minute	83.5±15	96.4±13.6	78.3±11.4	74.9±9.6	<0.001	<0.001	0.061
Aortic root diameter (cm)	3.44±0.34	3.45±0.37	3.47±0.31	3.38±0.33	0.677	0.110	0.035
Atrial Conduction times							
Lateral/mitral AEMD (msec)	55.6±17.3	71.2±13.6	52.8±10.4	41.2±12.4	<0.001	<0.001	<0.001
Lateral/tricuspid AEMD (msec)	27.3±14.3	41.2±12.7	22.5±8	16.9±8	<0.001	<0.001	<0.001
Septal AEMD (msec)	35.9±14.9	49.3±12.6	33.8±9.4	23±8.8	<0.001	<0.001	<0.001

The continuous variables are expressed as mean±standard deviation; RV: right ventricle; TAPSE: tricuspid annular plane systolic excursion; TD, tissue Doppler; TRV: tricuspid regurgitan velocity; SPAP: systolic pulmonary artery pressure; SM: systolic motion; LV: left ventricle; LVEF: left ventricle ejection fraction; AEMD: atrial electromechanical delay. Mann-Whitney-U test, Chi-square test.

($p < 0.001$). Lateral/mitral, lateral/tricuspid and septal AEMD were higher in Group 1 compared to other groups ($p < 0.001$).

Discussion

Acute exacerbation of COPD is the leading cause of morbidity and mortality.^[1] Inflammation in this period is expected to increase. In the study, CRP and CAR were higher and albumin was lower in acute exacerbation period and it was an expected finding for higher inflammation. CRP and albumin are frequently used biomarkers to measure inflammatory response and are known negative and positive acute phase reactants.^[16] The CRP/albumin ratio (CAR) is a more beneficial marker of the inflammatory process than CRP or albumin alone.^[16]

Our results suggest that in patients with acute COPD exacerbation, basal anterolateral, mid anterolateral, apicolateral, apex, apical septal, mid inferoseptal, basal inferoseptal strains and 4C-LS are decreased. Ventricular strain and strain rates, which are the deformation indicators of myocardium, are used for measurement of ventricular dysfunction.^[17] The LV consists of three non-homogenous fiber layers. Reverse positioning of subendocardial and subepicardial layer fibers is important for redistribution of the strain in the heart. Heterogenous deterioration of basal, middle and apical ventricular segments provide coordinated ventricular contraction. This LV contraction, which shows strain of the heart, can be impaired after decreased arterial oxygen saturation and increased negative intrathoracic pressure.^[18, 19] Severe hypoxia during acute exacerbation period may lead to decreased myocardial oxygenation, decreased LV contraction and decreased strain.

In the study, RV basal and mid diameters, Amax, Aa, TRV, SPAP, Amax mitral, Emax/Amax mitral, Aa (TD lateral mitral), heart rate were higher and RV vertical diameter, TAPSE, Emax/Amax, Ea/Aa, end-diastolic diameter, LVEF, Ea septum, Ea/Aa septum were lower in acute exacerbation period. In COPD patients, increased TRV is one of the result of increased SPAP.^[20, 21] Increased SPAP is caused by mechanical stress induced by hyperinflated lungs, hypoxia and impaired endothelial dysfunction in these patients.^[22] RV has a crescentic shape in echocardiographical practice.^[23] Increased pulmonary arterial pressure and wall stress in RV cause fibrosis, systolic-diastolic dysfunction and high oxygen consumption.^[24] The increased end-diastolic pressure with higher RV mass cause to ischemia and RV failure.^[24] COPD is one of the causes of increased pulmonary arterial pressure and acute exacerbation may impair right ventricular functions due to this increased pressure.^[3] Increased intrathoracic pressure for COPD patients reduces right

ventricular output, ventricular filling, stroke volume and cardiac output but dynamic changes in heart size throughout the respiration cycle has an unknown etiology.^[25] Increased intrathoracic pressure may also change right ventricular diameters. In COPD patients, the pressure caused by remodeling in the lung parenchyma causes changes in the right ventricle.^[26] TAPSE is used for evaluating degree of right ventricle function.^[26] Decreased TAPSE in patients with acute COPD shows impaired RV systolic function. In patients with COPD, the rate of Emax/Amax and Ea/Aa, indicating right ventricle diastolic function, is expected to decrease.^[5, 27] The right ventricle systolic and diastolic functions, which are thought to be more impaired in the acute COPD exacerbation patients, may cause these findings. LVEF, Ea/Aa mitral, and Ea/Aa septal were decreased in patients with acute COPD exacerbation. Inflammation is considered to be one of the systemic findings of COPD and this inflammatory reaction can cause atherosclerotic plaque formation, which is associated with myocardial ischemia, and left ventricular diastolic dysfunction. Impaired left ventricle diastolic function is associated with increased right ventricle pressure and volume load, showing that left ventricle diastolic functions are affected by right ventricle loading conditions.^[28, 29]

Another finding of the study is the significant prolongation of lateral/mitral, lateral/tricuspid and septal AEMD in acute exacerbation period. In COPD patients, inflammation, hypoxemia, hypercapnia, cardiac autonomic dysfunction, structural and functional changes of myocardium may trigger arrhythmias.^[30, 31] AF is the most common cardiac arrhythmia for these patients.^[30, 31] The prolonged AEMD is the predicting finding of AF.^[32, 33] COPD is independently related to AF, but well-known pathophysiological mechanisms are not completely comprehended.^[7] The right atrial dilatation, fibrosis, hypoxia, hypercapnia, oxidative stress, respiratory drugs such as beta agonists and anticholinergic agents may cause prolonged AEMD in COPD patients.^[7, 34] Prolonged AEMD may be result of increased inflammation in exacerbation period.

Study Limitations

This study was cross-sectional and patient follow-up could not be done. Long-term follow-up and large-scale prospective studies are needed to determine the predictive value of particularly AEMD in COPD patients. The presence of longitudinal strain images in only apical 4-chamber due to artefacts is another limitation of the study.

Conclusion

In conclusion, acute COPD exacerbation may cause prolonged AEMD, decreased longitudinal strain rates and im-

pairment of right-left ventricle systolic and diastolic functions compared to stable COPD patients.

Disclosures

Ethics Committee Approval: The study was approved by the Local Ethics Committee.

Peer-review: Externally peer-reviewed.

Conflict of Interest: None declared.

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