



Pulmonary Stiffness Significantly Increases in Patients with Chronic Obstructive Pulmonary Disease

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ABSTRACT

Objective: It was aimed to investigate whether there was a change in the pulmonary stiffness (PS) value detected by pulmonary elastography (PE) in patients with chronic obstructive pulmonary disease (COPD) and heart failure (HF) and to evaluate the utility of the PS value in the differential diagnosis of these diseases.

Material and Methods: The study included 20-healthy controls (Group-I) and 50-COPD (Group-II) and 50-HF patients (Group-III). In addition to routine examinations, PS of the patients was measured with PE.

Results: PS value was found to be significantly different between all groups, and Group II had the highest PS value ($p < 0.05$). PS values in Groups I-II-III were measured as 10.2 ± 1.4 kPa- 29.1 ± 6.8 kPa- 15.7 ± 3.8 kPa, respectively. It was also found that the PS value independently determined the presence of COPD ($p < 0.001$). According to this analysis, it was found that every 1 kPa rise increased the risk of having COPD by 85%. When 20 kPa was taken as the limit value in ROC curve analysis, it determined the patients with COPD with 96% sensitivity and 92.3% specificity. In addition, the measured PS values in COPD GOLD stages II-III-IV increased with the severity of the disease and found to be 25.5 ± 4.64 kPa, 29.5 ± 5.96 kPa, and 33.3 ± 9.85 kPa, respectively ($p < 0.001$).

Conclusion: In COPD and HF patients, more prominent in patients with COPD, the PS measured with PE increased. This PS elevation in COPD may be a novel differential diagnostic method in the differentiation of COPD patients from HF patients. In particular, the $PS > 20$ kPa can be used as a limit value for the differential diagnosis for COPD.

Keywords: Chronic obstructive pulmonary disease, heart failure, pulmonary elastography, pulmonary stiffness

ÖZ

Kronik Obstrüktif Akciğer Hastalığı Olan Hastalarda Pulmoner Sertlik Önemli Ölçüde Artmıştır

Giriş: Kronik obstrüktif akciğer hastalığı (KOAH) ve kalp yetmezliği (KY) olan hastalarda pulmoner elastografi (PE) ile tespit edilen pulmoner sertlik (PS) değerinde bir değişiklik olup olmadığını ve PS değerinin bu hastalıkların ayırıcı tanısında kullanılabilirliğini araştırmayı amaçladık.

Gereç ve Yöntemler: Çalışmaya 20 sağlıklı kontrol (Grup-I), 50 KOAH (Grup-II) ve 50 KY hastası (Grup-III) dahil edildi. Rutin muayenelere ek olarak PE ile hastaların PS'si ölçüldü.

Bulgular: PS değeri tüm gruplar arasında anlamlı olarak farklı bulundu ve Grup II en yüksek PS değerine sahipti ($p < 0.05$). Grup I-II-III'te PS değerleri sırasıyla 10.2 ± 1.4 kPa- 29.1 ± 6.8 kPa- 15.7 ± 3.8 kPa olarak ölçüldü. PS değerinin bağımsız olarak KOAH varlığını belirlediği bulundu ($p < 0.001$). Bu analize göre her bir kPa artışın KOAH riskini %85 artırdığı tespit edildi. ROC analizinde sınır değer olarak 20 kPa alındığında KOAH'lı hastaları %96 duyarlılık ve %92.3 özgüllük ile belirlediği saptandı. Ayrıca KOAH GOLD evre II-III-IV'te ölçülen PS değerleri hastalığın şiddeti ile artarak sırasıyla 25.5 ± 4.64 kPa, 29.5 ± 5.96 kPa ve 33.3 ± 9.85 kPa olarak bulundu ($p < 0.001$).

Sonuç: KOAH ve KY hastalarında, KOAH hastalarında daha belirgin olmak üzere, PE ile ölçülen PS artar. KOAH'daki bu PS yükselmesi, KOAH hastalarının KY hastalarından ayırt edilmesinde yeni bir ayırıcı tanı yöntemi olabilir. Özellikle $PS > 20$ kPa, KOAH ayırıcı tanısı için bir sınır değeri olarak kullanılabilir.

Anahtar Kelimeler: Kronik obstrüktif akciğer hastalığı, kalp yetmezliği, pulmoner elastografi, pulmoner sertlik

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INTRODUCTION

Chronic obstructive pulmonary disease (COPD) and heart failure (HF) are the most frequently diagnosed diseases in patients admitted to the emergency department with dyspnea. Smoking, old age, and increased systemic inflammation process are common risk factors for both diseases (1-3). In particular, differential diagnosis between COPD aggravation and HF decompensation may be uneasy. Therefore, this distinction is important for both treatment and hospitalization in the related department in patients admitted to the emergency department. Anamnesis, physical examination, lung radiography, natriuretic peptides, laboratory evaluation, echocardiography, pulmonary function test, and advanced imaging methods such as magnetic resonance imaging (MRI) can be used for differential diagnosis.

Although HF and COPD diseases produce similar symptoms, the pathophysiology that causes pulmonary disease in these diseases is different. In general lines; in patients with HF, increased left ventricular (LV) pressures increase pulmonary capillary wedge pressure (PCWP) and cause pulmonary symptoms by accumulating fluid in the alveolar area and in COPD patients, interstitial and submucosal edema, and fibrous remodeling can cause symptoms by airway compress and obstruction. Most of the techniques for differential diagnosis of these two diseases are not directly related to pulmonary parenchymal changes but are related to indirect or secondary causes. Pulmonary ultrasonography (US) examination is fast, non-invasive, repeatable and non-ionizing (4). Although it has been recently used in decompensated HF and some pulmonary diseases (5-9), it is still not used in COPD patients. Since the use of pulmonary US investigations starting in HF patients is not objective and not all ultrasonographers have the knowledge and experience about this usage, it is still not routinely used in HF diagnostic algorithm.

Elastography is a newly developed US technique that can quantify tissue stiffness and fibrosis development non-invasively and quantitatively. In recent years, elastography has become a common technique in the evaluation of solid organs such as kidneys, liver, testicles, prostate, thyroid, pancreas and breast. As far as we have investigated, there are studies in the literature using pulmonary elastography (PE) with US, but most of these studies investigate subpleural nodules or malignancy (10). Only, studies that involving a limited number of patients conducted by Zhang et al. (11-13) have shown increased pulmonary stiffness (PS) values in patients with interstitial lung disease (ILD) (11). We thought that there might be a secondary PS increase that caused by fibrous remodeling in the pathophysiology of COPD, and parenchymal compression with increased pressure in

the pulmonary parenchyma expanding in the fixed thorax musculoskeletal system. Similarly, increased alveolar fluid accumulation in HF patients may increase PS. Therefore, increased PS in these two diseases compared to normal lung parenchyma may be useful in clinical diagnosis and differential diagnosis.

In this study, we purposed to investigate whether there was a change in the PS value determined by PE in HF and COPD patients compared to the healthy control group and to evaluate the usability of the PS value in the differential diagnosis of these diseases.

MATERIALS and METHODS

Study Population

We included 50 patients with HF with reduced ejection fraction (36 males, 14 females and mean age of 64.9 ± 10.4 years) and 50 COPD patients with mildly-advanced and very advanced COPD (38 males, 12 females and mean age of 64.2 ± 6.8 years) who applied to the emergency service of our hospital with shortness of breath and 20 healthy controls similar in means of age and sex (mean age 62.3 ± 6.2 years and 14 males, 6 females) in this cross sectional study. The patients were evaluated by two different cardiologists and pulmonary disease specialists before the study. As a result of the examinations, patients who had dyspnea clearly related to COPD or HF were classified. In case of incompatibility with the diagnosis, the opinion of the cardiology professors who had more experience was obtained. We divided the patients into three groups as HF group, COPD group, and control group. Patients with severe renal failure (eGFR <30 ml/kg/ 1.73 m²), acute or chronic hepatic disease, severe valvular heart disease, inflammatory diseases, pneumonia, asthma bronchiole, pulmonary patients with embolism, hematological pathologies, active thyroid pathology, cancer and/or pregnancy, and patients who did not sign the informed consent form were excluded. Patients with COPD who had LV ejection fraction (EF) $<50\%$ and those with HF who had smoking history and FEV₁/FVC $<90\%$ were excluded from the study groups. In the control group, those with LVEF $<50\%$ and FEV₁/FVC $<90\%$ were excluded. The local ethics committee approved the study protocol (decision/protocol number of the ethics committee approval was 2018/292) and written informed consent was taken from each participant.

Afterwards, detailed history was collected, and physical examination was performed to all patients. Basal demographic features of all groups were obtained for sex, age, hypertension (HT), diabetes mellitus (DM) and active smoking. Heart rate, both systolic and diastolic blood pressures were documented. We calculated the body mass index (BMI)

by measuring weight and height. Hemoglobin, white blood cell (WBC), alanine aminotransferase, aspartate aminotransferase, creatinine, blood urea nitrogen (BUN), uric acid and N-terminal pro B-type natriuretic peptide (NT-proBNP) levels were also recorded.

Echocardiographic Examinations

Echocardiography measurements were performed on EPIQ 7 (Philips Healthcare Andover MA, USA). Images were taken according to the guidelines of the American Echocardiography Society (14). In parasternal long-axis M-mode measurement, LV systolic and diastolic lengths (LVd and LVs) were obtained. LVEF was measured by the modified Simpson technique from apical two and four chamber windows (15). Tricuspid regurgitation pressure gradient (TRPG) was obtained from the Bernoulli equation over the peak flow rate of tricuspid regurgitation. Right ventricular diastolic diameter (RVd) and tricuspid annular plane systolic excursion (TAPSE) was obtained from an RV focused apical four-chamber view.

Pulmonary Ultrasound

All patients and controls underwent pulmonary US screening using a high-resolution US device (Philips EPIQ 7) and a 5-1 MHz high-resolution convex probe (Philips Health Care, Bothell, WA, USA). The patients admitted to the emergency clinic were sent to the US laboratory for pulmonary US after hospitalization in Cardiology and Chest Diseases clinics' and after their intensive care unit treatment was completed. PS measurements were performed using the ElastPQ method, which is a point shear wave elastography (pSWE) assessment, with the patient in sitting position. Evaluation was made from the intercostal space with posterolateral approach. During pulmonary US, patients were asked to pause breathing for a few seconds to minimize pulmonary motion occurring with ventilation. The target area was defined, and the measurements were performed after the range of imaging (ROI) was located on the target (Figure 1). Pleural echogenicity and A lines were determined for ROI localization, and the ROI was taken as perpendicular to the pleural line between these two regions and from peripheral superficial parenchyma from the midline of the echogenicities of two adjacent costae. In our study, the maximum ROI target distance was 5 cm, with a constant ROI box dimension of 1 cm - 0.5 cm. In each patient, 12 valid measurements from different pulmonary lops were recorded, and their average was calculated. Firstly, three measurements were taken from the intercostal space from different regions of the right upper and right lower pulmonary lobe. Then, similar measurements were taken from the left upper and left lower pulmonary lobe. When the reliability of the measurement was low,

then the image would have a kPa of 0.00. The results were described in terms of kPa. Patients were evaluated by two highly experienced radiology specialists for conventional, SWE and Doppler examinations. Specialists had more than five years of experience in SWE studies and at least 500 SWE procedures in a year. All US examination durations were approximately 30 minutes.

Chronic Obstructive Pulmonary Disease Evaluation

Patients admitted to our hospital with acute aggravation of COPD were included in the study. Diagnosis of COPD was established according to the Global Initiative for Chronic Obstructive Lung Disease (GOLD) 2017 diagnostic criteria (16). Post bronchodilator spirometric measurement was performed in patients who have already been told how to do so while sitting 90 degrees upright, from the best of at least three spirometer samples with using Carefusion spirometer device (Würzburg, Germany). Patients were staged with GOLD 2017 COPD combined assessment system. The severity of this chronic airflow limitation was further classified based on the post-bronchodilator FEV_1 into GOLD stage 1 ($FEV_1 \geq 80\%$ of predicted value), GOLD stage 2 ($50\% < FEV_1 < 80\%$), GOLD stage 3 ($30\% < FEV_1 < 50\%$), GOLD stage 4 ($FEV_1 < 30\%$) (16).

Statistical Analysis

For all analyses, SPSS 23.0 statistical software pack (Chicago, IL, USA) was used. The variables were divided into groups: categorical and continuous. Normal distribution of the continuous variables was tested using Kolmogorov-Smirnov test. Continuous variables were expressed as mean \pm standard deviation if they were normally distributed. However, they were expressed as median (range) if not. Categorical variables were expressed as numbers and percentages. Continuous variables that showed normal distribution were compared using the Student t-test and ANOVA, whereas the Mann-Whitney U test and Kruskal-Wallis test were used for samples without normal distribution. The groups and their statistical comparisons were shown in tables. For the comparison of categorical variables, chi-square test was used. The chi-square (χ^2) test was used to compare categorical variables. In univariate analyses, the parameters that were significantly different in patients with COPD were determined. Then a logistic regression analysis was performed to determine the independent markers among patients with COPD showing differences. A receiver operator characteristic (ROC) curve analysis was performed to identify the optimal cut-off points of the PS for detecting COPD. The areas under curves were calculated to test the accuracies of the analyses. A p level of <0.05 was considered statistically significant.

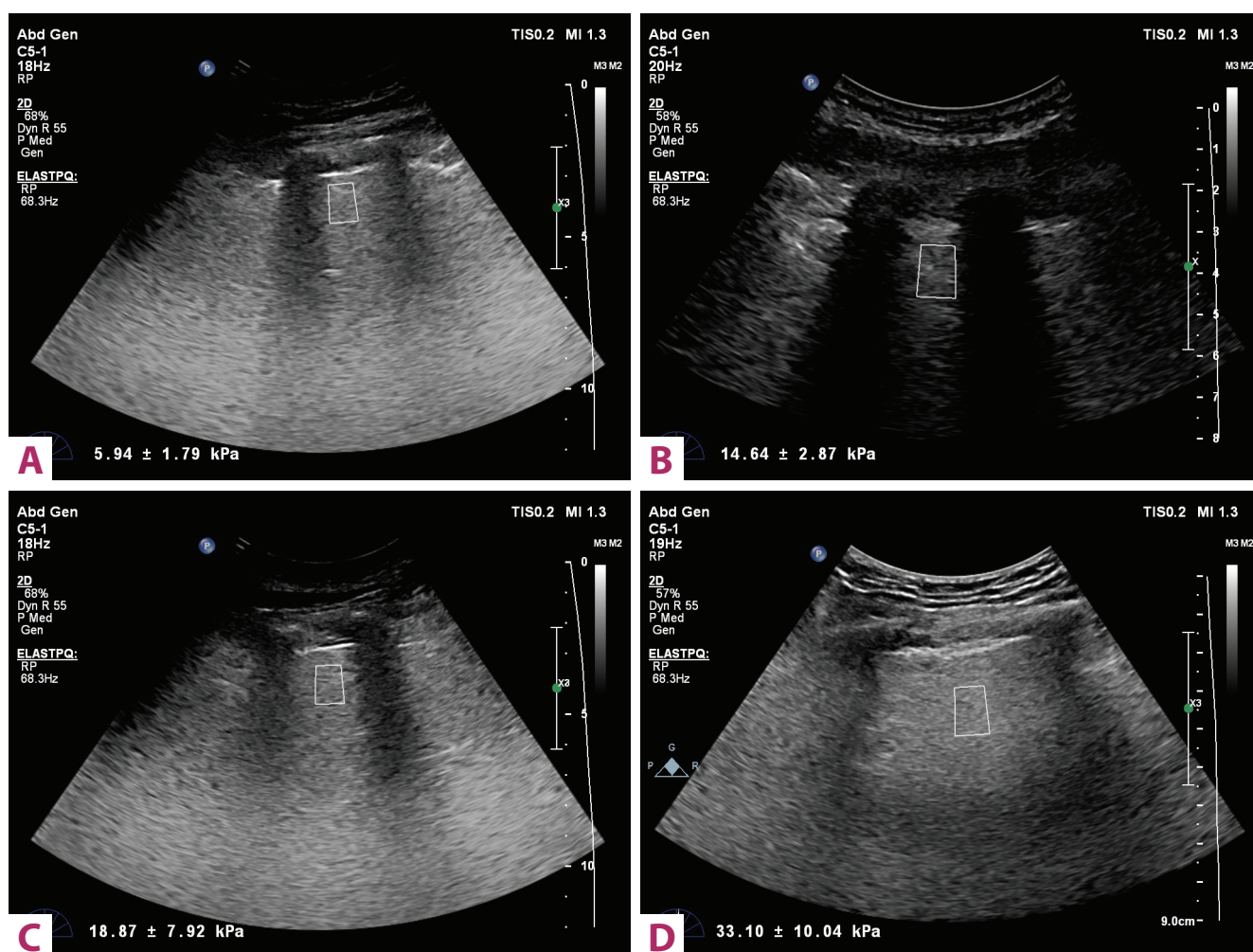


Figure 1. **A.** Pulmonary stiffness measurement by pulmonary elastography in control subject and normal pulmonary stiffness measurement in 5.94 ± 1.79 kPa is displayed in the lower left corner. **B.** Pulmonary stiffness measurement by pulmonary elastography in patients with HF and increased pulmonary stiffness measurement in 14.64 ± 2.87 kPa is displayed in the lower left corner. **C.** Pulmonary stiffness measurement by pulmonary elastography in patients with moderate COPD and increased pulmonary stiffness measurement in 18.87 ± 7.92 kPa is displayed in the lower left corner. **D.** Pulmonary stiffness measurement by pulmonary elastography in patients with severe COPD and severely increased pulmonary stiffness measurement in 33.10 ± 10.04 kPa is displayed in the lower left corner.

RESULTS

The study data were compared in three groups as control group (Group I), COPD group (Group II) and HF group (Group III). PS measurement was successfully obtained from all patients included in the study. Cohen kappa values that evaluate interobserver variability were over 90% for all echocardiographic and PS measurements.

Demographic, Clinical and Laboratory Data of the Study Groups

When demographic features were compared according to the study groups, age and sex were found to be similar in all groups. It was determined that all patients in Group III

were smokers, and the other two groups had no smokers and the presence of HT and DM was higher in Group III ($p < 0.05$), other clinical and demographic parameters were similar between the groups (Table 1). WBC and Hb levels were found to be the lowest in Group III patients; both parameters were significantly lower in the HF group than in the COPD group ($p < 0.05$ and Table 1). BUN, creatinine NT-proBNP and uric acid values were found to be elevated from Group I to Group III and found to be highest in Group III ($p < 0.05$ and Table 1). In the subgroup analysis, NT-proBNP, uric acid, BUN and creatinine levels in HF group were significantly higher than the COPD group and control group ($p < 0.05$). Other laboratory data were similar between the groups (Table 1).

Table 1. Clinical, demographic, laboratory and medical treatment findings according to study groups

Variable	Healthy controls n= 20	COPD patients n= 50	Heart failure n= 50	p
Age (year)	62.3 ± 6.2	64.2 ± 6.8	64.9 ± 10.4	0.496
Sex (male/female)	14/6	38/12	36/14	0.655
Hypertension, n (%)	-	4 (8%)	27 (54%)	0.002
Diabetes mellitus, n (%)	-	4 (8%)	19 (38%)	0.001
Current smoker, n (%)	-	50 (100%)	-	<0.001
SBP (mmHg)	120 ± 7.8 ^β	122 ± 10*	130 ± 11	<0.001
DBP (mmHg)	78 ± 13	80 ± 7.5	83 ± 8.9	0.071
Pulse (bpm)	75 ± 6.7	75 ± 9.3	79 ± 10	0.079
BMI (kg/m ²)	27.3 ± 3.0	27.5 ± 6.4	26.6 ± 5.7	0.736
Hemoglobin (g/dl)	13.2 ± 1.6 ^β	12.9 ± 1.6*	10.5 ± 1.3	<0.001
White blood cell (x10 ³ /μl)	8.9 ± 1.5 ^α	10.5 ± 2.8*	8.5 ± 2.9	0.001
AST (u/L)	22.8 ± 5.8	24.8 ± 9.4	26.5 ± 15.7	0.494
ALT (u/L)	24.6 ± 12.4	24.8 ± 15.1	24.0 ± 15.6	0.967
BUN (mg/dl)	29.4 ± 9.1 ^β	32.4 ± 10.9*	46.2 ± 20.8	<0.001
Creatinine (mg/dl)	0.75 ± 0.19 ^β	0.75 ± 0.20*	0.99 ± 0.27	<0.001
Uric aside	4.98 ± 1.01 ^β	5.17 ± 1.06*	6.56 ± 2.08	<0.001
NT-proBNP (pg/ml)	115 ± 90 ^β	191 ± 156*	3531 ± 2557	<0.001

ALT: Alanine aminotransferase, AST: Aspartate aminotransferase, BMI: Body mass index, BUN: Blood urea nitrogen, DBP: Diastolic blood pressure, hs-CRP: High sensitive C reactive protein SBP: Systolic blood pressure.

α: The significant association between the healthy controls group and COPD group (p< 0.05).

β: The significant association between the healthy controls group and heart failure group (p< 0.05).

*: The significant association between the heart failure group and COPD group (p< 0.05).

Table 2. Pulmonary ultrasound and echocardiographic findings according to study groups

Variable	Healthy controls n= 20	COPD n= 50	Heart failure n= 50	p
Lvd dimension (mm)	47.3 ± 4.4 ^β	48.1 ± 4.8*	62.9 ± 3.2	0.038
LVs dimension (mm)	30.9 ± 3.5 ^β	31.1 ± 4.3*	53.3 ± 3.9	0.005
LVEF (%)	61 ± 4.1 ^β	59.7 ± 5.2*	26.7 ± 5.7	0.002
RVd dimension (mm)	20.6 ± 3.8 ^β	31.4 ± 3.8*	23.6 ± 4.1	<0.001
TAPSE (mm)	18.7 ± 1.6 ^β	19.2 ± 1.81*	15.3 ± 1.4	<0.001
TRPG (mmHg)	19.9 ± 3.4 ^β	25.8 ± 7.5*	36.7 ± 6.3	<0.001
Pulmonary stiffness (kPa)	10.2 ± 1.4 ^{α,β}	29.1 ± 6.8*	15.7 ± 3.8	<0.001
Pulmonary stiffness ≥ 15 kPa, n (%)	0 (0%)	50 (100%)	27 (54%)	<0.001
Pulmonary stiffness ≥ 20 kPa, n (%)	0 (0%)	48 (96%)	5 (10%)	<0.001

LVEF: Left ventricular ejection fraction, LVD: Left ventricular diastolic, LVs: Left ventricular systolic, RVd: Right ventricular diastolic, TAPSE: Tricuspid annular plane systolic excursion, TRPG: Tricuspid regurgitation pressure gradient.

α: The significant association between the healthy controls group and COPD group (p< 0.05).

β: The significant association between the healthy controls group and heart failure group (p< 0.05).

*: The significant association between the heart failure group and COPD group (p< 0.05).

Echocardiographic Data of Study Groups

When the echocardiographic parameters were examined according to the study groups; LVD, LVs, RVd and TRPG values were the highest in Group III and significantly higher in the

HF group than in the COPD and control groups (p< 0.05 and Table 2). TAPSE and LVEF values were the lowest in Group III and significantly lower in the HF group than in the COPD and the control group (p< 0.05 and Table 2).

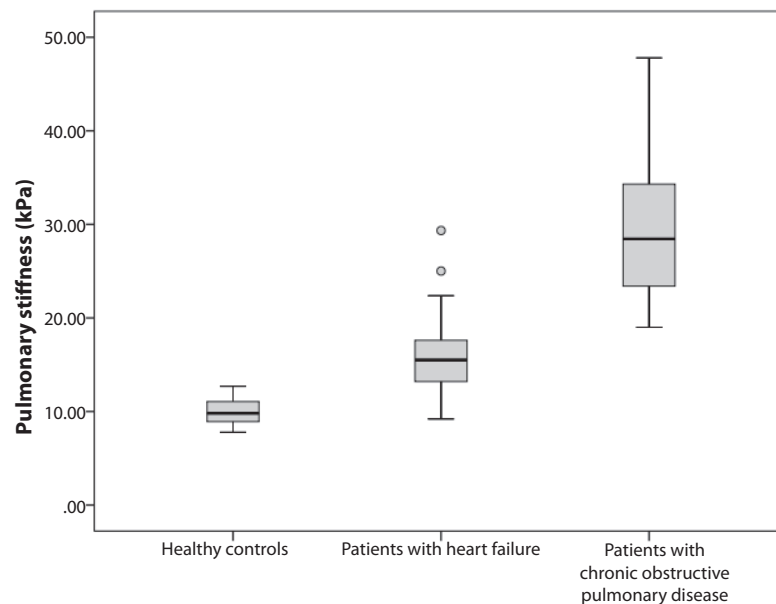


Figure 2. Pulmonary stiffness values according to study groups.

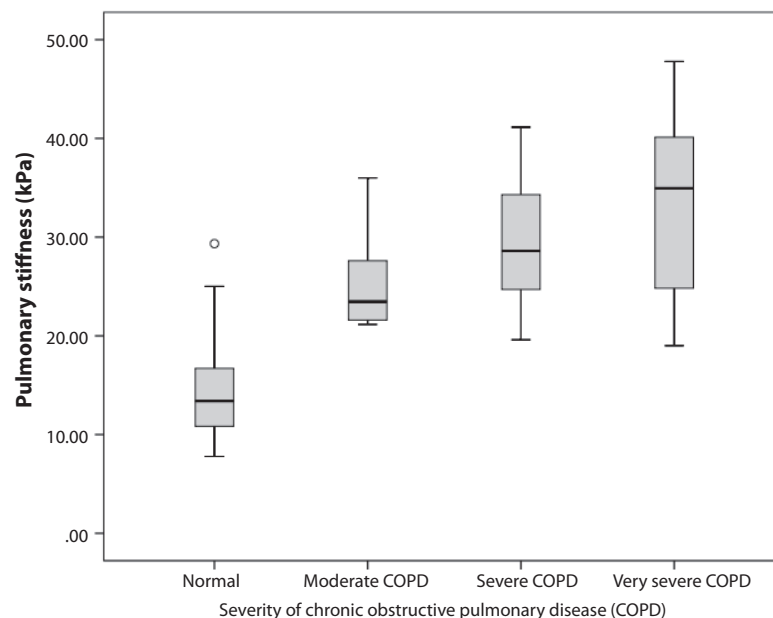


Figure 3. Pulmonary stiffness values according to COPD severity.

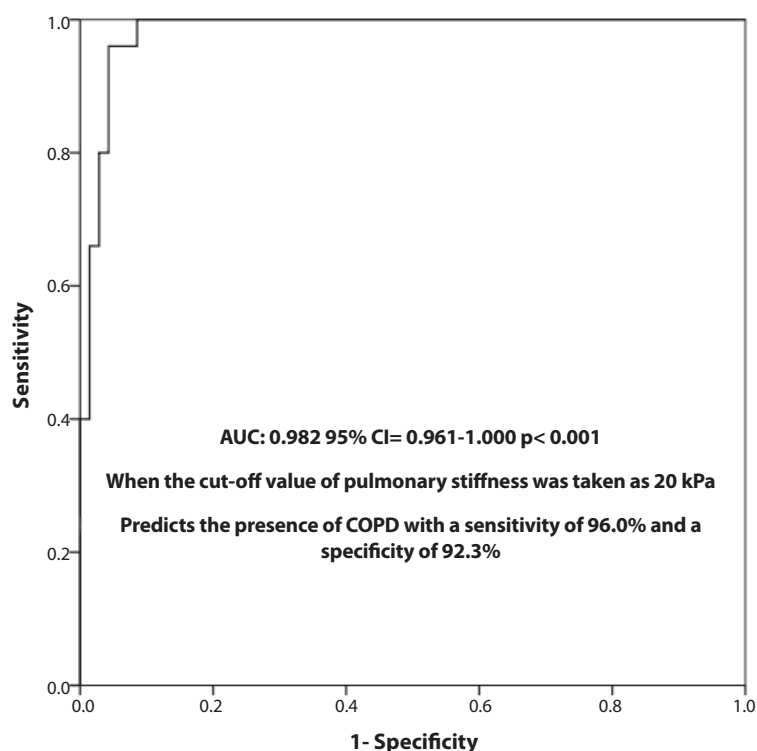
Pulmonary Elastography Data of Study Groups

When PE findings were compared between the study groups, PS value was found to be significantly different between all groups, PS values in the COPD group was significantly higher than the HF and control groups, and also HF group was significantly higher than the control group ($p <$

0.05, Table 2 and Figure 2). Having $PS \geq 15$ kPa and ≥ 20 kPa values were also found to be the most common in the COPD group (Table 2). Also, the measured PS values in COPD GOLD stage II-III-IV increased with the severity of the disease and found to be 25.5 ± 4.64 kPa, 29.5 ± 5.96 kPa and 33.3 ± 9.85 kPa, respectively ($p < 0.001$ and Figure 3).

Table 3. Independent parameters for the presence of chronic obstructive pulmonary disease

For > 7 kPa	Odds Ratio	95% Confidence Interval	p
Pulmonary stiffness (kPa)	1.850	1.424 – 2.402	<0.001

**Figure 4.** Receiver operating characteristic curves for pulmonary stiffness in the predicting of COPD.

The Relationship Between Pulmonary Stiffness and the Presence and Severity of COPD

When logistic regression analysis was performed to determine the patients with COPD, the PS value was determined the presence of COPD independently (Table 3). According to this analysis, an rise of 1 kPa increased the risk of COPD by 85%. A similar analysis was made with the ROC curve and the area under the ROC curve was found to be 0.982 ($p < 0.001$ and Figure 4). According to this analysis, when the limit value for PS was taken as 20 kPa, it determined the patients with COPD with a sensitivity of 96% and a specificity of 92.3%. In addition, 50 patients with COPD were grouped as moderate COPD (13 patients), severe COPD (29 patients) and very severe COPD (8 patients).

DISCUSSION

One of the main findings of this study was that the PS value obtained by PE in HF and COPD patients increased significantly compared to healthy controls. Most importantly, it

was determined that the PS value measured by noninvasive US examination in patients who presented with shortness of breath to the emergency department determined the presence of COPD better and independent than all parameters. When the limit value for PS is taken as >20 kPa, it determines the patients with COPD by acceptable sensitivity and specificity. Because of this close relationship, PS measurement and follow-up can be used as a COPD and HF distinction parameter in patients who present to the emergency department with dyspnea.

HF and COPD are two major problems in the modern world. Around 5-10% of the mature population has COPD GOLD II-IV (3). Ten to forty percent of the patients with HF also has COPD (3,17,18). The most important reason for this is that advanced age, smoking, physical activity, DM and increased inflammation are common risk factors in both HF and COPD patients (3). Therefore, COPD and HF differentiation should be performed clearly in order to provide faster and more effective treatment in patients with acute dyspnea.

Dyspnea, orthopnea, cough, muscle weakness and exercise intolerance are common symptoms in both HF and COPD patients. Right heart failure that could be seen in both diseases cause hepatomegaly, ankle edema and jugular venous pressure increase (1,3). Therefore, only anamnesis and physical examination are helpful in differential diagnosis, but their sensitivity and specificity are low. Electrocardiography is not specific for differential diagnosis. Chest radiography is helpful for diagnosis but does not make a definitive diagnosis and has low sensitivity and specificity (19). Of the natriuretic peptides, BNP and NT-proBNP are sensitive parameters for HF. HF is ruled out if the NT-proBNP value is <300 pg/ml (2). Although NT-proBNP sensitivity is 97%, its specificity is reported to be low and 47% (1,20). The high sensitivity of natriuretic peptides has been used in the differential diagnosis of dyspnea in the emergency department. However, it has been reported that there is an increase NT-proBNP in COPD patients (21). Echocardiography is used to evaluate cardiac functions and RV pressure in patients with COPD and HF. It is helpful in the diagnosis of HF, may indicate RV involvement in COPD patients, but it is not useful in COPD differential diagnosis. It is therefore difficult to give a precise limit to the differential diagnosis of HF and COPD.

Rapid evaluation and treatment should be performed in patients applying to the emergency room with dyspnea. The two most common diseases in the differential diagnosis of dyspnea in the emergency room are HF and COPD. There is no examination that is cheap, noninvasive, radiation free, and easy to perform for every radiologist in evaluation of pulmonary parenchyma in both COPD and HF patients. Pulmonary US is not among the routine evaluation of the patients admitted to the emergency room with dyspnea. There is no recommendation for pulmonary US examination in recent HF and COPD guidelines (16,22).

SWE assessment provides information about parenchymal stiffness of solid organs, especially the liver (23-25). SWE studies have shown especially that increased fibrosis and increased intra-organ pressure increase stiffness. SWE is used in many solid organ diseases, but there is not enough data on PS measurement due to the alveolar structure of the pulmonary parenchyma at the ROI sites and the problems in image acquisition from the intercostal space. However, in recent years, the increase in radiologist experience and the use of new techniques such as the ElastPQ technique, which has been successful in measuring almost all patients, has begun to be used in many new clinical situations. Especially, successful measurement can be obtained from intercostal space for right upper hepatic lobe in liver elastography (23-25).

In COPD patients, chronic bronchiolitis-induced obstructive condition causes interstitial and submucosal edema and fibrous remodeling. In addition to the resulting fibrosis remodeling, emphysema and hyperinflation occurs with alveolar destruction. Increased pulmonary volume in the thoracic space, which is fixed by the musculoskeletal system, causes pulmonary parenchymal compression due to the non-expandable thoracic space. In COPD patients, both fibrous degeneration and pulmonary pressure increase are expected to increase pulmonary stiffness compared to normal pulmonary parenchyma. Therefore, the PS value measured in COPD patients may be useful in the differential diagnosis of these patients. This finding has been demonstrated in US, computed tomography and MRI elastography studies (11-13,26,27).

As we investigated, i) Pulmonary US elastography studies in previous ILD patients ii) The importance of tissue stiffness obtained with SWE in non-pulmonary organs iii) our clinical experience (23-25) suggested that the PS value obtained with SWE should be evaluated in patients with COPD and HF. We successfully obtained PS measurement from all patients and controls included in our study. Therefore, the PS value obtained with a mean of at least 12 different measurements may be a new follow-up parameter that can objectively demonstrate the stiffness of the pulmonary parenchyma. Non-invasively determining the PS value in both HF and COPD patients will provide important information for follow-up and medication. In a study conducted by Zhang et al. (12) in 2011, it was shown for the first time that PS values measured by PE were increased in pulmonary disease patients. After this preliminary study, Zhang et al. (11,13) reported successful PS measurement in the studies published in 2016-2017 and the PS value was significantly higher in the patient group. In the previous study, a PS value determined with 100 Hz of 3.3 ± 0.37 m/s in ILD patients was reported. In addition, SWE technique was used in this study (11-13). In this study, high-resolution US device and a pSWE examination, a state-of-art system ElastPQ method, was used. In this study, we found that the mean PS value was 29.1 ± 6.8 kPa in COPD patients with 68.3 Hz. PS was successfully recorded from all patients. Although there are different LE measurement methods, the most important feature of the ElastPQ method used in our study is the ease of use and the possibility of taking high rate of accurate measurements. The most important distinctions of our study from the studies conducted by Zhang et al. (11-13) are the count of cases included in the study, the disease status and purpose, as well as the PS measurement technique. Although the control group and ILD patients were evaluated in the previous study, involvement the HF and COPD patients, who were frequently confused in the

emergency department and were sometimes challenged in the differential diagnosis, made it more important than the previous study.

Pulmonary US examination is fast, non-invasive, repeatable and non-ionizing (4). Recently, the increased use of pulmonary US in decompensated HF (5), pneumonia (6), pneumothorax (7), pulmonary embolism (8), and pleural effusion (9) have been used to diagnose patients with high sensitivity and specificity. There is no elastography study, except that a PS increase determined with SWE is shown to increase in a limited number of ILD patients (11,13). Pulmonary elastography is mostly used in the differential diagnosis of malignant and benign lesions in peripheral pulmonary lesions (28,29), but not in COPD patients. In our study, PS was the highest in COPD patients compared to both control and HF patients. When it was taken as 20 kPa limit value for PS, it was determined that patients with COPD with 96% sensitivity and 92.3% specificity were determined. PS value was found to be associated with COPD disease severity as well as detection of COPD patients. It was found to be 25.5 ± 4.64 kPa, 29.5 ± 5.96 kPa and 33.3 ± 9.85 kPa in COPD GOLD stages II-III-IV, respectively. In our study, it was found that every 1 kPa increase in PS value increased the risk of being COPD by approximately 85%. These findings suggest that PE can have a new area of use.

Our study has some important limitations. In our study, 50 patients with HF and 50 patients with COPD were enrolled, which may be insufficient for these groups of patients with very different clinical features and risk factors. Our study is a single-center study, but the result is very ambitious. Therefore, a multicentric study involving more patients is required. The diseases studied in our study, HF and COPD, are isolated diseases. As known, both HF and COPD involve common risk factors such as smoking, old age, and increased systemic inflammation process (1). Our study is more important in the differential diagnosis of COPD disease and may not give clear information about whether HF is present or not and could not help to exclude HF. We did not perform spirometer evaluation, procalcitonin, exercise test and blood gas analysis in all study groups. It could be more meaningful if these tests were performed. All patients in our study had decompensated diseases, and their first evaluation was made in the emergency department. Findings were made in this group of patients, and chronic follow-up patients should be studied. Due to the use of the ElastPQ technique, no limitation could be compared with another study. Also, patients in our study were not followed up for prognosis.

CONCLUSION

COPD and HF are common in clinical practice. Early diagnosis of these patients is very important for planning treat-

ment. In COPD and HF patients, more prominent in patients with COPD, the PS measured with PE increases. The PS value determined by non-invasive pulmonary US independently determines the presence of COPD in patients presenting to the emergency room with dyspnea. PS measurement could be used as a cheap, simple and non-invasive parameter for diagnosis, differential diagnosis and follow-up of COPD and HF patients. According to the results of our study, > 20 kPa for PS determined in pulmonary US may be predictive for the presence of COPD. These results in our study are very important in COPD and HF distinction and can be used and applied in clinics easily. However, it was concluded that the results obtained in this study should be strengthened by new multicentric studies including larger, different patient groups.

Main Points

- i. In COPD patients, the PS value increases that measured with PE.
- ii. The PS value measured by non-invasive pulmonary US independently determines the presence of COPD in patients presenting to the emergency department with dyspnea.
- iii. PS examination could be used as a simple, cheap, and non-invasive parameter for diagnosis, differential diagnosis and follow-up of COPD and HF patients.

Ethics Committee Approval: The study was approved from Adana City Training and Research Hospital Clinical Research Ethics Committee (Date: 28.08.2019 Decision No: 534).

Author Contributions: Concept/Design: All of authors; Analysis/ Interpretation: All of authors; Data Acquisition: All of authors; Writing: HK; Critical Revision: All of authors; Final Approval: All of authors.

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REFERENCES

1. de Miguel Díez J, Chancafe Morgan J, Jiménez García R. The association between COPD and heart failure risk: a review. *Int J Chron Obstruct Pulmonal Dis* 2013;8:305-12.
2. Horodinschi RN, Bratu OG, Dediu GN, Pantea Stoian A, Motofei I, Diaconu CC. Heart failure and chronic obstructive pulmonary disease: a review. *Acta Cardiol* 2020;75(2):97-104.
3. Hawkins NM, Virani S, Ceconi C. Heart failure and chronic obstructive pulmonary disease: the challenges facing physicians and health services. *Eur Heart J* 2013;34(36):2795-803.
4. Sforza A, Mancusi C, Carlino MV, Buonauro A, Barozzi M, Romano G, et al. Diagnostic performance of multi-organ ultrasound with pocket-sized device in the management of acute dyspnea. *Cardiovasc Ultrasound* 2017;15(1):16.

5. Al Deeb M, Barbic S, Featherstone R, Dankoff J, Barbic D. Point-of-care ultrasonography for the diagnosis of acute cardiogenic pulmonary edema in patients presenting with acute dyspnea: a systematic review and meta-analysis. *Acad Emerg Med* 2014;21(8):843-52.
6. Chavez MA, Shams N, Ellington LE, Naithani N, Gilman RH, Steinhoff MC, et al. Lung ultrasound for the diagnosis of pneumonia in adults: a systematic review and meta-analysis. *Respir Res* 2014;15:50.
7. Alrajab S, Youssef AM, Akkus NI, Caldito G. Pleural ultrasonography versus chest radiography for the diagnosis of pneumothorax: review of the literature and meta-analysis. *Crit Care* 2013;17(5):R208.
8. Squizzato A, Rancan E, Dentali F, Bonzini M, Guasti L, Steidl L, et al. Diagnostic accuracy of lung ultrasound for pulmonary embolism: a systematic review and meta-analysis. *J Thromb Haemost* 2013;11(7):1269-78.
9. Vignon P, Chastagner C, Berkane V, Chardac E, François B, Normand S, et al. Quantitative assessment of pleural effusion in critically ill patients by means of ultrasonography. *Crit Care Med* 2005;33(8):1757-63.
10. Mostbeck G. Elastography everywhere - now even the lungs! *Ultraschall Med* 2014;35(1):5-8.
11. Zhang X, Osborn T, Zhou B, Meixner D, Kinnick RR, Bartholmai B, et al. Lung ultrasound surface wave elastography: a pilot clinical study. *IEEE Trans Ultrason Ferroelectr Freq Control* 2017;64(9):1298-1304.
12. Zhang X, Qiang B, Hubmayr RD, Urban MW, Kinnick R, Greenleaf JF. Noninvasive ultrasound image guided surface wave method for measuring the wave speed and estimating the elasticity of lungs: A feasibility study. *Ultrasonics* 2011;51(3):289-95.
13. Zhang X, Osborn T, Kalra S. A noninvasive ultrasound elastography technique for measuring surface waves on the lung. *Ultrasonics* 2016;71:183-8.
14. Sahn DJ, DeMaria A, Kisslo J, Weyman A. Recommendations regarding quantitation in M-mode echocardiography: results of a survey of echocardiographic measurements. *Circulation* 1978;58(6):1072-83.
15. Lang RM, Bierig M, Devereux RB, Flachskampf FA, Foster E, Pellikka PA, et al. Recommendations for chamber quantification: a report from the American Society of Echocardiography's Guidelines and Standards Committee and the Chamber Quantification Writing Group, developed in conjunction with the European Association of Echocardiography, branch of the European Society of Cardiology. *J Am Soc Echocardiogr* 2005;18(12):1440-63.
16. Vogelmeier CF, Criner GJ, Martinez FJ, Anzueto A, Barnes PJ, Bourbeau J, et al. Global strategy for the diagnosis, management, and prevention of chronic obstructive lung disease 2017 report. GOLD executive summary. *Am J Respir Crit Care Med* 2017;195(5):557-82.
17. Iversen KK, Kjaergaard J, Akkan D, Kober L, Torp-Pedersen C, Hassager C, et al. ECHOS-Lung Function Study Group. Chronic obstructive pulmonary disease in patients admitted with heart failure. *J Intern Med* 2008;264(4):361-9.
18. Boschetto P, Fucili A, Stendardo M, Malagù M, Parrinello G, Casimiri E, et al. Occurrence and impact of chronic obstructive pulmonary disease in elderly patients with stable heart failure. *Respirology* 2013;18(1):125-30.
19. Cardinale L, Volpicelli G, Lamorte A, Martino J, Andrea Veltri. Revisiting signs, strengths and weaknesses of standard chest radiography in patients of Acute Dyspnea in the Emergency Department. *J Thorac Dis* 2012;4(4):398-407.
20. Roberts E, Ludman AJ, Dworzynski K, Al-Mohammad A, Cowie MR, McMurray JJ, et al. NICE Guideline Development Group for Acute Heart Failure. The diagnostic accuracy of the natriuretic peptides in heart failure: systematic review and diagnostic meta-analysis in the acute care setting. *BMJ* 2015;350:h910.
21. Labaki WW, Xia M, Murray S, Curtis JL, Barr RG, Bhatt SP, et al. NT-proBNP in stable COPD and future exacerbation risk: Analysis of the SPIROMICS cohort. *Respir Med* 2018;140:87-93.
22. Ponikowski P, Voors AA, Anker SD, Bueno H, Cleland JGF, Coats AJS, et al. ESC Scientific Document Group. 2016 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure: The Task Force for the diagnosis and treatment of acute and chronic heart failure of the European Society of Cardiology (ESC) developed with the special contribution of the Heart Failure Association (HFA) of the ESC. *Eur Heart J* 2016;37(27):2129-200.
23. İçen YK, Demirtaş AO, Koç AS, Sümbül HE, Koç M. Liver stiffness value obtained with ElastPQ ultrasound increases with NYHA class in chronic heart failure patients and reduced ejection fraction. *Türk Kardiyol Der* 2019;47(4):281-93.
24. Bankir M, Sumbul HE, Koc AS, Demirtas D, Acibucu F. Elastography detected solid organ stiffness increased in patients with acromegaly. *Medicine (Baltimore)* 2019;98:e14212.
25. Koç AS, Sumbul HE. Prediabetes is associated with increased liver stiffness identified by noninvasive liver fibrosis assessment: ElastPQ Ultrasound Shear Wave Elastography Study. *Ultrasound Q* 2019;35(4):330-8.
26. Marinelli JP, Levin DL, Vassallo R, Carter RE, Hubmayr RD, Ehman RL, et al. Quantitative assessment of lung stiffness in patients with interstitial lung disease using MR elastography. *J Magn Reson Imaging* 2017;46(2):365-74.
27. Hasse K, O'Connell D, Min Y, Neylon J, Low DA, Santhanam A. Estimation and validation of patient-specific high-resolution lung elasticity derived from 4DCT. *Med Phys* 2018;45(2):666-77.
28. Wei H, Lu Y, Ji Q, Zhou H, Zhou X. The application of conventional us and transthoracic ultrasound elastography in evaluating peripheral pulmonary lesions. *Exp Ther Med* 2018;16(2):1203-8.
29. Sperandeo M, Trovato FM, Dimitri L, Catalano D, Simeone A, Martines GF, et al. Lung transthoracic ultrasound elastography imaging and guided biopsies of subpleural cancer: a preliminary report. *Acta Radiol* 2015;56(7):798-805.