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RESEARCH

Relationship between arterial stiffness and pulmonary artery pressure in patients with COPD

KOAH'lı hastalarda arteriyel sertlik ve pulmoner arter basıncı arasındaki ilişki

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Abstract

Purpose: By impacting both the vascular bed and the airways, endothelial damage brought on by chronic inflammation in COPD may hasten the onset of pulmonary hypertension (PH). The purpose of the study that was presented was to look into the connection between arterial stiffness and the onset and intensity of pulmonary hypertension in COPD.

Materials and Methods: Data from patients who were diagnosed with COPD between 2016 and 2022 served as the basis for this retrospective investigation. Clinical, radiologic, pulmonary function, and sociodemographic information were documented. Measurements of arterial stiffness were conducted using data from the literature. Based on the results of echocardiogram (ECHO), patients were split into two groups: those with and without high systolic pulmonary artery pressure (es_PAP). The pertinent data were then examined.

Results: The mean age of the 224 COPD patients in our study was 60.45 ± 9.59 years, and 89.3% of them were male. In our investigation, the prevalence of es_PAP was 41.5%. 9.4% of patients passed away. es_PAP was found to be connected with a mean age of 64.60 years and older, living alone, frequent hospitalization, and employment status. Additionally, it is discovered that mean 6-minute walk test (6MWT) distance of 340 meters or less, mean body mass index (BMI) of 24.45 or less, mean waist circumference of 94 cm or less, mean BODE score of 3.66 or more, mean depression score of 4.73 or more, and stage 3–4 Medical Research Council (MRC) levelwas linked to es_PAP.

Conclusion: Although arterial stiffness, the severity of COPD, and es_PAP did not significantly correlate in our study, the conditions and risk factors that we did discover to be linked to es_PAP should be regularly monitored and well managed.

Keywords:. COPD, arterial stiffness, pulmonary hypertension, mortality, pulmonary function tests

Öz

Amaç: KOAH'ta kronik inflamasyonun neden olduğu endotel hasarı, vasküler yatağın yanı sıra hava yollarını da etkileyerek pulmoner hipertansiyon (PH) gelişimini hızlandırabilir. Çalışmamızda, KOAH hastalarında arteriyel sertlik ile PH gelişimi ve şiddeti arasındaki ilişkiyi araştırmayı planladık.

Gereç ve Yöntem: Bu çalışma 2016-2022 yılları arasında KOAH tanısı alan hastaların verilerine dayanan retrospektif bir çalışmadır. Sosyodemografik veriler, klinik, radyolojik ve solunum fonksiyon bulguları kaydedildi. Arteriyel sertlik ölçümleri literatür verilerine göre yapıldı. Hastalar ekokardiyografi (EKO) bulgularına göre pulmoner arter basıncı artmış olanlar ve olmayanlar olarak 2 gruba ayrılarak risk faktörleri ve ilgili bulgular analiz edildi.

Bulgular: Çalışmamıza dahil edilen 224 KOAH hastasının %89,3'ü erkek ve yaş ortalaması 60,45 ± 9,59 idi. Çalışmamızda artmış sistolik pulmoner arter basıncı (es_PAP) prevalansı %41,5 idi. Olguların %9,4'ü öldü. Ortalama yaşın 64.60 ve üzeri olması, yalnız yaşama, sık hastaneye yatma ve çalışma durumunun es_PAP ile ilişkili olabileceği bulunmuştur. Ayrıca evre 3-4 tıbbi araştırma konseyi (MRC) düzeyi, ortalama 340 metre ve altında 6 dakikalık yürüme testi (6DYT) mesafesinin, vücut kitle indeksinin (VKİ) ortalama 24.45 ve altında, bel çevresinin ortalama 94 cm ve altında, ortalama BODE skorunun 3.66 ve üzerinde, ortalama depresyon skorunun 4.73 ve üzerinde olmasının es_PAP ile ilişkili olabileceğini bulduk.

Sonuç: Çalışmamızda arteriyel sertlik ile KOAH şiddeti ve es_PAP arasında anlamlı bir ilişki bulamadık. Ancak es_PAP ile ilişkili olarak bulduğumuz durumlar ve risk faktörleri açısından daha yakından takip edilmeli ve iyi yönetilmelidir.

Anahtar kelimeler: KOAH, arteriyel sertlik, pulmoner hipertansiyon, mortalite, solunum fonksiyon testleri

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INTRODUCTION

The term "chronic obstructive pulmonary disease" (COPD) refers to a variety of conditions that are characterized by persistent and frequently progressive airway blockage, as well as chronic respiratory symptoms including coughing, sputum production, and dyspnea brought on by abnormalities of the airways or alveoli[1]. The most important determinants of disease course and mortality are the severity of airway stenosis, exacerbations, and concomitant diseases[1].

Cardiovascular diseases, diabetes mellitus, metabolic syndrome, osteoporosis, osteopenia, lung cancer, cachexia, anemia, depression, stroke, and cognitive decline are significant comorbidities linked to COPD[2]. Cardiovascular diseases are the most common comorbidities, leading causes of hospitalization, and death in patients with COPD. Therefore, there is a close link between COPD and cardiovascular diseases. Systemic inflammation, elevated oxidative stress, neurohumoral abnormalities, and an increased propensity for thrombosis are some possible reasons of increased cardiovascular disease risk in COPD[3].

In order to improve risk analysis in COPD and more accurately predict cardiovascular events and death, cardiovascular risk scores are measured in conjunction with lung function testing[4]. Some subclinical markers such as carotid intima-media thickness, endothelial function and arterial stiffness have been studied in cardiovascular diseases. It was concluded that arterial stiffness, in particular, may be a strong predictor of cardiovascular events and may be more useful in routine clinical practice than other measures[5]. Arterial stiffness in COPD has been linked independently to the severity of the disease as well as to oxidative stress, inflammation, and elevated sympathetic activity—all of which are key mechanisms by which COPD causes vascular remodeling and, subsequently, cardiovascular events. Furthermore, elevated systemic inflammation and sympathetic activity are frequently linked to exacerbations of COPD, and both of these factors contribute to the development of arterial stiffness[6,7].

This study was designed with the hypothesis that elevated arterial stiffness in COPD may be a short-term indicator of disease severity. On the basis of available data and possible mechanisms, we aimed to examine the link between this condition and pulmonary hypertension (PH) and to contribute to the literature by determining the incidence and risk factors of PH development in COPD patients.

MATERIALS-METHODS

Study design

This retrospective study was conducted by including 224 patients who were admitted to the chest diseases clinic of a university hospital between April 2016 and December 2022 and diagnosed with COPD based on clinical findings and lung function tests. Approval for the project was received from the Cukurova University Faculty of Medicine Non-Interventional Clinical Research Ethics Committee (approval number 124/2022). The 1964 Helsinki Declaration and the hospital's and the national research committee's ethical guidelines were followed in all activities involving human participants during the study. Informed consent was obtained from all participants for the study.

Sample

The study was conducted by physicians with academic competence working in the pulmonology clinic of a tertiary university hospital where interventional and clinical practices are performed and data security is high.

Inclusion criteriawere being over 40 years of age, diagnosed with COPD based on clinical, radiological and pulmonary function tests (PFTs) findings and echocardiography (ECHO) was performed during follow-up, without peripheral arterial/venous disease and without structural lung disease (interstitial lung disease, bronchiectasis, cystic fibrosis, etc.)

Exclusion criteria were those who did not meet the inclusion criteria, those with increased pulmonary artery pressure due to a cause other than COPD and those with missing data

It was planned to include 294 patients in the study, but 70 patients were excluded from the study, including 16 patients with peripheral arterial/venous disease, 14 patients with structural lung disease, 22 patients with increased pulmonary artery pressure due to a cause other than COPD, and 18 patients with missing data. The study was conducted with 224 patients. In order to reach the most accurate result in cases where the PH rate in COPD patients is around 15% on average in the literature, we needed

to include at least 196 patients in our study according to the results of the power analysis we conducted with a 5% margin of error and a 95% confidence interval.

Procedure

Among the patients with retrospective data, those who died during the study period were identified by telephone or through the interhospital data recording system and recorded in this way. Sociodemographic findings such as age, gender, educational and income status, occupation, marital status, clinical findings such as smoking history (pack/year), body mass index (BMI), comorbidities, and laboratory findings such as complete blood count and biochemical tests were recorded from the hospital data system.

COPD diagnosis and severity assessment

When pulmonary function tests (PFTs) were conducted on patients suspected of having COPD based on clinical and radiological signs, irreversible airway blockage was found, leading to the diagnosis of the condition. PFTs were performed in the PFT laboratory and evaluated according to standard reference values determined in international ATS/ERS guidelines. Patients were divided into GOLD-ABE groups using the current GOLD 2024 report on COPD severity.

In the study, the modified medical research council (mMRC) dyspnoea classification was used for dyspnoea severity, the 6-minute walking test (6-MWD) distance measurement for exercise capacity, and the BODE index ((B) body mass index; (O) forced expiratory volume in one second (FEV1) for airflow obstruction; (D) dyspnoea measurement with the mMRC scale; and (E) exercise capacity measurement with the 6-minute walking distance (6-MWD)) for disease severity[1].

Pulmonary Artery Pressure and Arterial stiffness assessment

According to recent updates, the definitive diagnosis of PH is made with a mean pulmonary artery pressure (mPAP) >20 mmHg on right heart catheterization[9]. Since catheterization is an invasive and expensive diagnostic tool, it is more appropriate to use ECHO, a noninvasive, easily applicable and cost-effective method to guide PH. Although ECHO does not make a definitive diagnosis of PH, it guides the clinician in terms of PH by measuring systolic pulmonary artery pressure (sPAP). Based on this, although a sPAP >25 mmHg is not sufficient for the diagnosis of pulmonary hypertension, we will express this result as elevated systolic pulmonary artery pressure (es_PAP) in our study[9].

Arterial stiffness is defined as the hardening of the arteries. It is computed using pulse wave velocity (PWV), which takes into account the artery wall's anatomical dimensions and inherent elasticity. The PWV is the ratio of the distance (m) to the transit time (s) between two pressure waves that were transcutaneously measured at two different artery locations. A practical and secure noninvasive technique for determining central arterial stiffness is arterial PWV. The European Society of Hypertension and the European Society of Cardiology, in particular, regard carotid-femoral PWV as the gold standard[10,11]. Its application in clinical trials and daily practice is supported by its reliability as an indicator of future cardiovascular events and all-cause death[10,11]. Another method, pulse pressure difference (PP), the difference between systolic and diastolic pressure, can be used as a rough and indirect indicator of stiffness[12].

Statistical analysis

To do statistical analyses, SPSS version 22.0 (SPSS, Inc. Chicago, Illinois) was utilized. Kolmogorov-Smirnov test was used for normal distribution properties of variables. Parametric tests were preferred for quantitative data conforming to normal distribution, and nonparametric tests were preferred for nonconforming data and categorical data. Mean and standard deviation (SD) of parametric data were reported. Two-sided t-test for normally distributed data and two-sided Mann-Whitney-U test for non-normally distributed data were used to analyze group differences. Median and quartile range were shown for continuous data and mean ± SD for regularly distributed data. Chi-square tests were used to compare percentage summaries of categorical variables. The t test, Mann-Whitney-U test and chi-square tests were used to determine the relationship between arterial stiffness and es_PAP in COPD patients. P values less than 0.05 were considered statistically significant.

RESULTS

Two hundred and twenty-four COPD patients were included in our study and the prevalence of es_PAP among these patients was 41.5%. The mean age of

our patients was 60.45 ± 9.59 and 89.3% were male. es_PAP was observed in older patients (mean age 64.60 ± 9.48) and this was statistically significant (p=0.002). During the study, 9.4% of the cases died, and although es_PAP was observed in 57.1% of those who died, no relationship was found between death and es_PAP (p=0.127). We observed that 60% of those living alone had es_PAP and that marital status may be associated with es_PAP (p=0.047). We also determined that employment status; especially in retirees, es_PAP develops more frequently than in other employees (73.1% of all cases) and that this situation may be associated with es_PAP (p=0.005). During the follow-up period, 12.1% of the cases were hospitalized and treated, and 62.9% of the patients had es_PAP, which was statistically significant (p=0.016). The most common comorbidity was hypertension (HT) with a rate of 28.6%, and no significant relationship was found between comorbidities and es_PAP. Detailed sociodemographic-clinical characteristics of the cases are presented in table 1.

Table 1. Relationship between sociodemographic and clinical characteristics and elevated systolic pulmonary artery pressure

Variables		**n (%) or mean ± SD**			**Value**	**p**
		Total (n=224)	Group 1 (es_PAP) (n=93)	Group 2 (non-es_PAP) (n=131)		
Age		60.45 ± 9.59	64.60 ± 9.48	60.45 ± 9.59	*-3.207	**0.002**
Sex	Male	200 (89.3)	86 (92.5)	114 (87)	ᵉ1.689	0.194
	Female	24 (10.7)	7 (7.5)	17 (13)		
Smoke	Yes	133 (59.4)	55 (59.1)	78 (59.5)	ᵉ0.004	0.952
	No	91 (40.6)	38 (40.9)	53 (40.5)		
Lives	Yes	203 (90.6)	81 (87.1)	122 (93.1)	ᵉ2.330	0.127
	No	21 (9.4)	12 (12.9)	9 (6.9)		
Marital status	Married	199 (88.8)	78 (83.9)	121 (92.4)	ᵉ3.959	**0.047**
	Single	25 (11.2)	15 (16.1)	10 (7.6)		
Hospitalization	Yes	27 (12.1)	17 (18.3)	10 (7.6)	ᵉ5.815	**0.016**
	No	197 (87.9)	76 (81.7)	121(92.4)		
Readmission	Yes	14 (6.2)	8 (8.6)	6 (4.6)	ᵉ1.502	0.220
	No	210 (93.8)	85 (91.4)	125 (95.4)		
Heart failure	Yes	26 (11.6)	13 (14)	13 (9.9)	ᵉ0.872	0.371
	No	198 (88.4)	80 (86)	118 (90.1)		
DM	Yes	13 (5.8)	4 (4.3)	9 (6.9)	ᵉ0.657	0.418
	No	211 (94.2)	89 (95.7)	122 (93.1)		
HT	Yes	64 (28.6)	26 (28)	38 (29)	ᵉ0.029	0.864
	No	160 (71.4)	67 (72)	93 (71)		
Chronic Kidney Disease	Yes	4 (1.8)	3 (3.2)	1 (0.8)	ᵉ1.880	0.170
	No	220 (98.2)	90 (96.2)	130 (99.2)		
Chronic Liver disease	Yes	3 (1.3)	1 (1.1)	2 (1.5)	ᵉ0.084	0.772
	No	221 (98.7)	92 (98.9)	129 (98.5)		
Rheumatological Diseases	Yes	4 (1.8)	2 (2.2)	2 (1.5)	ᵉ1.766	0.779
	No	220 (98.2)	91 (97.8)	129 (98.5)		
Peripheral Vascular Disease	Yes	8 (3.6)	5 (5.4)	3 (2.3)	ᵉ1.504	0.220
	No	216 (96.4)	88 (94.6)	128 (97.7)		
GOLD Stage	A	43 (19.2)	14 (15.1)	29 (22.1)	ᵉ2.474	0.290
	B	82 (36.6)	33 (35.5)	49 (37.4)		
	E	99 (44.2)	46 (49.5)	53 (40.5)		
Working Status	Unemployed	47 (21)	12 (12.9)	35 (26.9)	ᵉ14.672	**0.005**
	Housewife	19 (8.5)	7 (7.5)	12 (9.2)		
	Employee	17 (7.6)	3 (3.2)	14 (10.4)		
	Farmer	4 (1.8)	3 (3.2)	1 (0.8)		
	Retired	137 (61.2)	68 (73.1)	69 (62.7)		

Abbrevations: es_PAP: elevated systolic pulmonary artery pressure, DM: Diabetes Mellitus, HT: Hypertension, ᵉ: Chi-square test, *: Mann whitney U test, ᵃ: T test

In our study, we found that the parameters in respiratory function tests, forced expiratory volume in the 1st second before bronchodilation (preFEV1 (L)), forced expiratory volume percentage in the 1st second after bronchodilation (postFEV1 (%)) and carbon monoxide diffusion tests percentage (DLCO (%)), may have a significant relationship with es_PAP (p=0.019, p=0.047, p=0.004, respectively). The relationship between the parameters in respiratory function tests and es_PAP is presented in table 2.

Table 2. Relationship between elevated systolic pulmonary artery pressure and respiratory function tests

Variables (mean ± SD)	Total (n=224)	Group 1 (es_PAP) (n=93)	Group 2 (non-es_PAP) (n=93)	t Value	p
PreFEV1 (L)	1.59 ± 0.62	0.58 ± 0.06	0.64 ± 0.05	[a]2.355	**0.019**
PostFEV1 (L)	2.08 ± 0.53	0.63 ± 0.06	7.21 ± 0.63	[a]1.345	0.181
PreFEV1 (%)	54.13 ± 19.71	52.09 ± 18.85	55.59 ± 20.24	[a]1.327	0.186
PostFEV1 (%)	58.65 ± 19.53	55.53 ± 20.44	60.87 ± 18.62	[a]1.997	**0.047**
PreFVC (L)	3.32 ± 2.41	3.20 ± 2.12	3.39 ± 2.85	[a]0.254	0.800
PostFVC (L)	3.97 ± 2.49	3.81 ± 2.91	4.08 ± 2.35	[a]0.222	0.825
PreFVC (%)	71.61 ± 21.51	69.80 ± 21.65	72.89 ± 21.38	[a]1.061	0.290
PostFVC (%)	79.02 ± 19.31	76.24 ± 20.54	80.98 ± 18.21	[a]1.783	0.076
PreFEV1/FVC (%)	57.65 ± 9.11	56.56 ± 9.03	58.42 ± 9.12	[a]1.515	0.131
PostFEV1/FVC (%)	57.18 ± 9.49	55.85 ± 9.45	58.13 ± 9.44	[a]1.785	0.076
DLCO (%)	57.79 ± 17.51	53.85 ± 17.25	60.59 ± 17.20	[a]2.884	**0.004**

Abbrevations: es_PAP**:** elevated systolic pulmonary artery pressure, PreFEV1 (L): Forced expiratory volume in the 1st second before bronchodilation, PostFEV1 (L): Forced expiratory volume in the 1st second after bronchodilation, PreFEV1 (%): Forced expiratory volüme percentage in the 1st second before bronchodilation, PostFEV1(%): Forced expiratory volüme percentage in the 1st second after bronchodilation, PreFVC (L): Forced vital capacity before bronchodilation, PostFVC (L): Forced vital capacity after bronchodilation, PreFVC (%): Forced vital capacity percentage before bronchodilation, PostFVC (%): Forced vital capacity percentage after bronchodilation, PreFEV1/FVC (%): Percentage of FEV1/FVC before bronchodilation, PostFEV1/FVC (%):Percentage of FEV1/FVC after bronchodilation, DLCO (%): Carbon monoxide diffusion tests percentage, a: T test

We found that medical research council (MRC) and 6-minute walk test (6MWT), which are indicators of dyspnea severity, may be associated with es_PAP (p=0.011, p=0.025, respectively). We found that the incidence of es_PAP increased especially in MRC stage 4 and the 6MWT distance was shorter in COPD patients with es_PAP. We observed that body mass index may also be associated with es_PAP, and es_PAP is more common in underweight COPD patients (p=0.000). In addition, the waist circumference of COPD patients with es_PAP was thinner and this was statistically significant (p=0.006). We found that the mean BODE scores associated with disease severity in COPD patients were higher in those with es_PAP and that this was significant for es_PAP (p=0.002). Another important finding was that the mean depression score was higher in those with es_PAP, and we found that this was statistically significant (p=0.005). Parameters and measurements that may be related to disease severity and clinical progression in COPD patients are presented in detail in table 3.

Table 3. Relationship between clinical evaluations and technical measurements and elevated systolic pulmonary artery pressure

Variables (n (%) or mean ± SD)	Total (n=224)	Group 1 (es_PAP) (n=93)	Group 2 (non-es_PAP) (n=93)	Value	p
MRC Grade 1	54 (24.1)	20 (21.5)	34 (26)	[é]13.039	**0.011**
MRC Grade 2	113 (50.4)	42 (45.2)	71 (54.2)		
MRC Grade 3	23 (10.3)	10 (10.8)	13 (9.9)		
MRC Grade 4	17 (7.6)	14 (15.1)	3 (2.3)		
MRC Grade 5	17 (7.6)	7 (7.5)	10 (7.6)		
6MWT	374.19 ± 210.21	340.41 ± 128.94	398.17 ± 250.27	[a]2.254	**0.025**
BMI	25.88 ± 4.48	24.45 ± 4.17	26.90 ±4.42	[a]4.214	**0.000**
BODE Stage	3.06 ± 2.49	3.66 ± 2.73	2.63 ± 2.23	[a]-3.076	**0.002**
Waist Circumference	96.69 ± 11.37	94.14 ± 12.06	98.49 ± 10.52	[a]2.800	**0.006**
Waist-Hip Ratio	0.93 ± 0.09	0.92 ± 0.07	0.93 ± 0.11	[a]0.920	0.359
Anxiety	4.71 ± 4.35	5.20 ± 4.54	4.36 ± 4.18	[a]-1.418	0.158
Depression	3.81 ± 4.12	4.73 ± 4.52	3.16 ± 3.70	[a]-2.851	**0.005**
BNP	192.70 ± 407.05	228.02 ± 477.17	167.63 ± 348.65	[a]-1.039	0.300
Arterial Stiffness	482.05 ± 324.27	507.86 ± 393.13	463.73 ± 264.92	[a]-0.941	0.348
Cardiac Injury score	14.06 ± 6.65	15.05 ± 6.86	13.36 ±6.42	[a]-1.861	0.064

Abbrevations: es_PAP**:** elevated systolic pulmonary artery pressure, MRC: Medical research council, 6MWT: 6 minute walk test, BODE: Body mass index-Airflow Obstruction-Dyspnea-Exercise capacity, BMI: Body mass index, BNP: Brain natriuretic peptide, [é]: Chi-square test, [a]: T test

DISCUSSION

In our study, we found that the all-cause es_PAP rate in COPD patients was 41.7%, and the mortality rate was 57.1% in those with es_PAP compared to those without es_PAP. Advanced age, living alone, retirement status, hospitalization, pulmonary function test parameters such as low PreFEV1 (L), low PostFEV1 (%) and low DLCO (%), advanced MRC, decreased 6MWT, low BMI, increased BODE stage, decreased waist circumference, depression diagnosis and medication use were found to be associated with es_PAP in COPD patients. However, the relationship between arterial stiffness and COPD severity or the presence of es_PAP in COPD patients could not be determined.

There is no clear data in the literature regarding the prevalence of PH due to COPD. Although there are different study results, it has been reported that the prevalence may increase up to 50% in selected populations[13-16]. In various studies in patients with severe airway obstruction, it was reported that 90% of these patients had mPAP > 20 mmHg[14,16], while another study reported that only 3-5% of this group had mPAP ranges above 35-40 mmHg[17]. The definitive diagnosis of PH is right heart catheterization. However, it is a rare, invasive and expensive diagnostic tool. Therefore, it is not applied to every COPD patient in daily practice. Considering the prevalence of COPD, it is more appropriate to use ECHO, which is a noninvasive, easily applicable and cost-effective method for PH. Although ECHO does not provide a definitive diagnosis of PH, it measures systolic pulmonary artery pressure and guides the clinician in terms of PH. In this respect, it is a valuable examination. In our study, we defined the elevations in systolic pulmonary artery pressure measured by ECHO as elevated systolic pulmonary artery pressure (es_PAP), and in this way, we found the rate of es_PAP due to all etiological causes among our patients to be 41.7%.

The relationship between arterial stiffness and COPD has been investigated in some studies. McAllister et al reported that the severity of

emphysema in COPD patients was associated with arterial stiffness independent of airflow limitation and systemic inflammation[6]. According to a different study, cigarette smoke and aberrant endothelium function had no bearing on the rise in arterial stiffness associated with COPD[18]. PWV was shown to be independently correlated with age, cigarette pack size, and FEV1, and arterial stiffness in COPD was found to be higher than in controls, with a significant increase in severe COPD[19]. Sabit et al.[20] 36 stable COPD patients and 14 healthy adults, left ventricular dysfunction was associated with arterial stiffness and right ventricular dysfunction was associated with airway obstruction in COPD. In our study, we found that mean arterial stiffness was increased in patients with es_PAP compared to patients with normal pulmonary artery pressure, but not statistically significant. This result was interpreted as arterial stiffness does not provide sufficient information about right ventricular function, as in limited studies in the literature. However, it should be supported by randomized controlled studies with larger patient participation.

PH disease progression in COPD patients is very important as it is directly linked to quality of life and mortality. In the analysis of data records of 10,165 patients with COPD and PH between July 2007 and August 2020 with the participation of 62 centers from 12 different countries; the main variables associated with transplantation or death in patients with PH in COPD were determined as advanced age, male gender, low 6MWT, high mPAP, high PVR and high NT pro-BNP[21]. Another study investigating 84 patients who underwent right heart catheterization immediately before initiation of long-term oxygen therapy in COPD patients reported an inverse correlation between mPAP and/or PVR values and survival. The same study showed that in COPD patients with PH >25 mmHg, the 5-year survival rate was significantly reduced and pulmonary hemodynamics had a greater prognostic impact on survival than FEV1, degree of hypoxemia, or hypercapnia[22]. In a study conducted between 2010 and 2017 and including 750 COPD patients, they stated that 5-year mortality rates were significantly higher in the PH group than in the non-PH group and that age, BMI, FEV1, and especially the FVC/DLCO ratio were independent predictors of 5-year all-cause mortality[23]. There are limited studies in the literature examining the association of living alone or social isolation with PH. A 2018 study examined the association of social deprivation with prognosis in Scottish patients with idiopathic PH (IPAH) or hereditary PH (HPAH)[24]. The study showed that patients in the IPAH/HPAH group were more socially deprived than other Scottish citizens, but this did not have a positive or negative contribution to prognosis[24]. A meta-analysis published in 2023 examined the association of loneliness, social isolation or living alone with mortality risk in individuals with established cardiovascular disease[25]. This meta-analysis found that different results were reached in the studies examined in this meta-analysis, that there were partially biased studies, but ultimately found that loneliness, social isolation or living alone were associated with an increased risk of early death[25]. In our study, we found that advanced age, frequent hospitalizations, increased lung function loss, MRC stage 4, decreased 6MWT, low BMI, increased BODE stage, and decreased waist circumference were associated with es_PAP in COPD patients in accordance with the literature. We also found that the risk of es_PAP increased in COPD patients with social and financial isolation, such as living alone, retirement status, and depression, and we observed that there is limited data in the literature on this subject.

In addition to the strengths and positive aspects of our study, such as the high number of patients, long-term follow-up and the fact that it was performed only in a tertiary care institution, there are also weaknesses and limitations, such as being based on retrospective data, being performed in a single center and not being able to perform pulmonary artery catheterization, which is the gold standard in the diagnosis of PH.

In conclusion, this study did not find an association between arterial stiffness and COPD severity and elevated systolic pulmonary artery pressure. On the other hand, although we found similar results with previous studies in terms of PH risk factors, we found that living alone and retirement and depression may be associated with es_PAP due to COPD. We think that this is important in terms of the limited data on this subject in the literature. Considering that arterial stiffness may be a predisposing factor for many vascular diseases and pulmonary hypertension may be an important cause of morbidity and mortality in COPD, we suggest that this issue should be evaluated in a multicenter and larger patient cohort, especially in terms of incidence and possible risk factors.

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