

The role of penile elastography in the evaluation of erectile dysfunction in patients with chronic obstructive pulmonary disease

Mustafa Gurkan Yenice¹, Yavuz Onur Danacioglu¹, Rustu Turkey², Cagla Pinar Tastan³, Ebru Artan³, Emre Sam⁴, Abdulmuttalip Simsek⁵, Ali Ihsan Tasci¹

¹Department of Urology, University of Health Sciences, Bakirkoy Dr. Sadi Konuk Training and Research Hospital, Istanbul, Turkey

²Department of Radiology, University of Health Sciences, Haseki Training and Research Hospital, Istanbul, Turkey

³Department of Chest Diseases, University of Health Sciences, Bakirkoy Dr. Sadi Konuk Training and Research Hospital, Istanbul, Turkey

⁴Department of Urology, University of Health Sciences, Regional Training and Research Hospital, Erzurum, Turkey

⁵Department of Urology, Basaksehir Cam ve Sakura City Hospital, Istanbul, Turkey

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Corresponding author

Emre Sam

University of Health Sciences

Erzurum Regional Training and Research Hospital

Department of Urology

Cat Yolu Street

25400 Erzurum, Turkey

phone: +90 537 839 4767

emresam@yahoo.com

Introduction In this study, we aimed to measure the change in penile stiffness by evaluating corpus cavernosum (CC) with shear wave elastography (SWE) in patients with chronic obstructive pulmonary disease (COPD).

Material and methods Seventy outpatient patients aged 50–80 years who were diagnosed with COPD were evaluated using SWE. Patients were divided into 2 groups according to the International Index of Erectile Function-5 (IIEF-5) questionnaire (IIEF-5 >17: Group A, IIEF-5 <17: Group B). The measurements were made in both transverse and longitudinal sections.

Results The mean age of the patients was 60 ±7.9 years. The duration of COPD was significantly higher in Group B than in Group A ($p = 0.003$). The mean SWE values of right transverse mid-portion of corpus penis (RTM) and left transverse mid-portion of corpus penis (LTM) in Group B (21.1 ±5.6 kPa and 20.8 ±4.8 kPa, respectively) were significantly higher than in Group A (15.2 ±2.3 kPa and 15.8 ±2.7 kPa, respectively); ($p < 0.001$ and $p < 0.001$, respectively). There was a significant negative correlation between IIEF-5 scores and the duration of COPD ($p < 0.05$). There was a significant negative correlation between IIEF values and RTM and LTM values of the patients ($p < 0.05$ and $p < 0.05$, respectively). There was a significant positive correlation between the duration of COPD and both RTM and LTM values ($p < 0.05$ and $p < 0.05$, respectively).

Conclusions In our study, according to the SWE findings, we showed the effect of systemic changes created by COPD on penile tissue and the negative effect of this on erectile function in patients.

Key Words: erectile dysfunction ↔ impotence ↔ elastography ↔ chronic obstructive pulmonary disease

INTRODUCTION

Chronic obstructive pulmonary disease (COPD) is a common, preventable, and treatable disease characterized by persistent respiratory symptoms that develop as a result of exposure to harmful particles or gases, resulting in abnormalities of the airways or alveoli [1]. It is a chronic systemic disease that is not limited to the airways; it has various effects on the human body,

such as other chronic systemic diseases [2, 3]. In patients with COPD, dyspnea, cough, muscular weakness, and decreased physical activity affect patients' daily functioning to varying degrees according to the effort capacity, and also disrupt sexual activity [4]. The psychosocial, vascular, inflammatory, and endocrinologic disorders caused by COPD's feature of being a chronic disease, besides its somatic-physical effect on health status, may cause erectile dysfunction

tion (ED) [5, 6]. However, ED may be neglected by physicians in patients with moderate and mild COPD, whose health status is not impaired. The risk of developing ED in patients with COPD is higher than in patients with other comorbidities; the prevalence of ED is 72% to 87% in patients with moderate to severe COPD [7, 8]. Eighty-seven percent of patients with COPD disregard sexual problems and do not discuss these problems with their physicians, and 78% do not share their sexual problems concerning their/ with their partners [9].

Shear wave elastography (SWE) is a non-invasive test which quantitatively evaluates the elasticity of tissues. The SWE probe sends acoustic impulses to create molecular vibrations in tissue, and these vibrations cause shear waves in tissue. The spreading velocity of shear waves gives information about tissue elasticity [10, 11]. SWE provides effective results about breast, thyroid, prostate, and liver diseases, and therefore it has been addressed in various studies to evaluate various organs and pathologies [12]. In order to form an erection, the innervation and structure of the corpus cavernosum (CC) and endocrine system must be healthy, and the blood flow to the genital system and sinusoidal tissue compliance must be sufficient [13]. For this reason, evaluation of the structure of CC may be important in terms of predicting ED and regulating appropriate treatment. We have limited methods in ED diagnosis, such as the self-reported International Index of Erectile Function (IIEF-5) questionnaire form. SWE may be used as a new noninvasive diagnostic method in the diagnosis and prediction of ED. The objective of this study was to investigate the efficacy of SWE for the diagnosis of ED in patients with COPD and its effects on CC structure of COPD.

MATERIAL AND METHODS

Seventy outpatient patients who were aged 50–80 years, had a heterosexual relationship, and were diagnosed as having COPD according to the Global Initiative for Chronic Lung Disease (GOLD) criteria were included in the study between January 2016 and December 2018 [1]. The ethics committee of our hospital approved this prospective study (2016/46), and informed consent was obtained from all patients. The clinical findings, demographic characteristics, smoking status (pack/year amount or ex-smoker), and the duration of COPD were evaluated. All patients underwent standard spirometry, forced vital capacity (FVC), forced expiratory volume in 1 second (FEV1), and FEV1/FVC were evaluated using spirometry (Spirolab III S/N A23-053, Rome, Italy). The stages of COPD were accepted as mild (FEV1 >80%), moder-

ate (FEV1 50–80%), severe (FEV1 30–50%), and very severe (FEV1 <30%), according to the GOLD criteria. Patients included in the study had moderate (FEV1 50–80%) or severe (FEV1 30–50%) COPD and patients with mild and very severe COPD were excluded because the patients with very severe COPD may not be suitable for sexual intercourse and the mild patient group was not included in the study to form a pure patient group [1]. A physical examination was performed on all patients. Patients with Peyronie's disease, penile trauma history, penile surgery for any reason, other serious systemic diseases, active oncologic disease, endocrinologic or psychological disorders were excluded. None of the patients had been undergoing treatment with phosphodiesterase 5 (PDE-5) inhibitors or systemic corticosteroids. Evaluation and classification of sexual functions of the patients were performed using the IIEF-5 (self-reported) questionnaire, which has been validated in Turkish [14]. The maximum score is 25 points, and classification is as follows: 5–11 points, severe; 12–16 points, moderate; 17–21 points, mild; and 22–25 points, no ED [15]. The patients were divided into 2 groups based on the IIEF-5 scores. Thirty-five volunteers with no erectile dysfunction (IIEF-5 score >17) or none of the exclusion criteria comprised the control group (Group A). Thir-

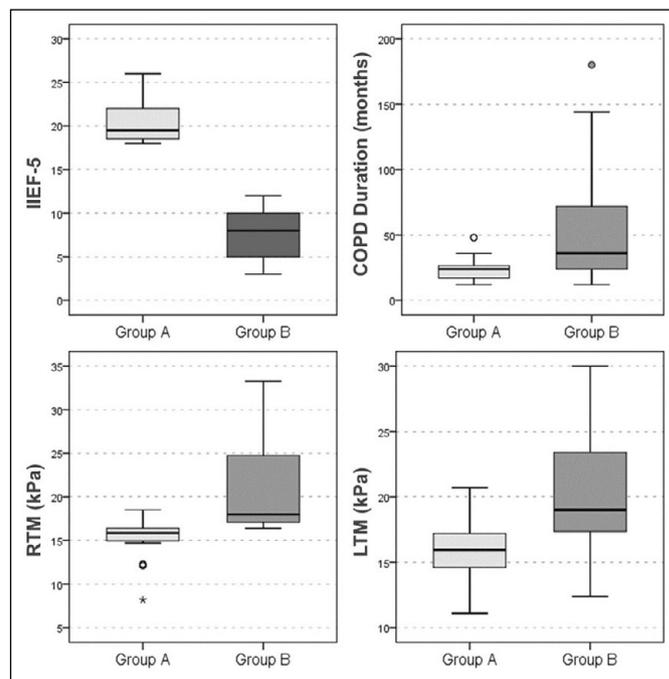


Figure 1. The median values of IIEF-5, COPD duration, SWE values of the right and left corpus cavernosum between the groups.

COPD – chronic obstructive pulmonary disease; RTM – right transverse mid-portion of corpus penis; LTM – left transverse mid-portion of penile corpus; IIEF-5 – International Index of Erectile Function



Figure 2. Sonographic transverse image of 65-year-old-man with COPD. Circle demonstrates elastographic measurement of RTM in kPa. The patient's elastographic measurement was 16 kPa.

COPD – chronic obstructive pulmonary disease; RTM – right transverse mid-portion of penile corpus; kPa – kilo Pascal

ty-five patients with IIEF-5 scores <17 were included in Group B. In each group, SWE was performed by an experienced sonographer (R.T.) using a linear transducer (12–16 MHz) with an Aplio 500 platinum (Toshiba, Tokyo, Japan) ultrasonography device (Figures 1 and 2). All patients were laid in the supine position and the measurements were performed from the middle part of the penis while the penis was in a flaccid state and the probe was placed in the transverse axis during measurement. The ROI circle was placed 1 cm deep on the CC of the penis. Five measurements were made for each patient separately and the average was calculated for the final SWE value. The measurement results were noted in kilo Pascal (kPa) units. The differences of measurements between the two groups were analyzed statistically.

Statistical analysis

The statistical analysis was performed using the Statistical Package for the Social Sciences Ver. 22.0 software package (SPSS, Chicago, USA). In descriptive statistics, the data are given as mean, standard deviation, median, and minimum and maximum. The distribution of variables was measured using the Kolmogorov-Smirnov test. The independent sample t-test and Mann-Whitney-U test were used in the analysis of independent quantitative data.

RESULTS

The mean age of the patients was 60 ± 7.9 years, and the mean ages of the patients in Group A and

Group B were 57.5 ± 6.1 years and 62.1 ± 8.7 years, respectively ($p = 0.061$). The demographic data of the patients are summarized in Table 1. There was no difference between the groups in terms of mean ages, body mass index (BMI) values, smoking durations, FEV1 values, and FEV1/FVC values ($p > 0.05$). The mean IIEF-5 scores in groups A and B were 20.5 ± 2.4 vs 7.6 ± 3.0 , respectively. The duration of COPD was significantly longer in Group B than in Group A (57.3 ± 47.3 months vs 24.1 ± 10.6 months) ($p = 0.003$). The mean SWE values of right transverse mid-portion of corpus penis (RTM) and left transverse mid-portion of corpus penis (LTM) in Group B (21.1 ± 5.6 kPa and 20.8 ± 4.8 kPa) were significantly higher than in Group A (15.2 ± 2.3 kPa and 15.8 ± 2.7 kPa); ($p < 0.000$) ($p < 0.001$) (Table 2). There was a significant negative correlation between the IIEF-5 values and the duration of COPD according to the correlation analysis ($p < 0.05$). In addition, there was a significant negative correlation between the IIEF-5 values and RTM and LTM values ($p < 0.05$ and $p < 0.05$, respectively). There was a significant positive correlation between the duration of COPD and both RTM and LTM values ($p < 0.05$ and $p < 0.05$, respectively) (Table 3) (Figure 1).

DISCUSSION

This study examined the use of SWE in the diagnosis of ED and the changes that COPD, which is a chronic and progressive disease, creates on CC structure. As a result, it was determined that COPD duration was positively correlated with SWE value and negatively correlated with IIEF-5. This indicates that the changes caused by COPD on CC may lead

Table 1. The demographic features of the patients

	Minimum-Maximum	Median	Mean \pm SD
Age (year)	50–83	60	60 \pm 7.9
BMI (kg/m ²)	19.4–42.6	25.8	26.8 \pm 4.8
Smoking time (year)	20–80	35	35.2 \pm 11.1
COPD duration (months)	12–180	24.5	40.7 \pm 37.8
FEV1	3–76	56	56.9 \pm 11.9
FEV1/FVC	49–69	63	61.5 \pm 6.4
RTM (kPa)	8.2–33.3	16.8	18.1 \pm 5.2
LTM (kPa)	11.1–30	17.4	18.3 \pm 4.6
IIEF-5	3–26	15	14 \pm 7

BMI – body mass index; COPD – chronic obstructive pulmonary disease; FEV1 – forced expiratory volume in 1 second; FVC – forced vital capacity; RTM – right transverse mid-portion of penile corpus; LTM – left transverse mid-portion of penile corpus; IIEF-5 – International Index of Erectile Function; SD – standard deviation; kPa – kilo Pascal

Table 2. Comparison of patient characteristics in both groups

	Group A		Group B		p
	Mean \pm SD	Median	Mean \pm SD	Median	
Age (year)	57.5 \pm 6.1	57	62.1 \pm 8.7	61	0.061 ^t
BMI (kg/m ²)	26.5 \pm 5.1	25.6	27.1 \pm 4.7	25.9	0.675 ^m
Smoking time (year)	36.5 \pm 13.5	35	34 \pm 8.2	34	0.713 ^m
COPD duration (months)	24.1 \pm 10.6	24	57.3 \pm 47.3	36	0.003 ^m
FEV1	56.3 \pm 13.2	57.5	55.6 \pm 11	55	0.482 ^m
FEV1/FVC	61.7 \pm 7.2	64	61.4 \pm 5.9	61.5	0.776 ^m
RTM (kPa)	15.2 \pm 2.3	15.9	21.1 \pm 5.6	18	0.000 ^m
LTM (kPa)	15.8 \pm 2.7	16	20.8 \pm 4.8	19	0.000 ^m
IIEF-5	20.5 \pm 2.4	19.5	7.6 \pm 3	8	0.000 ^m

BMI – body mass index; COPD – chronic obstructive pulmonary disease; FEV1 – forced expiratory volume in 1 second; FVC – forced vital capacity; RTM – right transverse mid-portion of penile corpus; LTM – left transverse mid-portion of penile corpus; IIEF-5 – International Index of Erectile Function; ^t – Sample T test; ^m – Mann-Whitney U test; kPa – kilo Pascal; SD – standard deviation

Table 3. Correlation results of IIEF-5 scores and COPD duration between COPD duration and RTM and LTM values

	COPD duration (months)	RTM (kPa)	LTM (kPa)
IIEF-5			
r	-0.449	-0.676	-0.486
p	0.004	0.000	0.001
COPD duration (months)			
r	–	0.348	0.269
p		0.028	0.093

COPD – chronic obstructive pulmonary disease; RTM – right transverse mid-portion of penile corpus; LTM – left transverse mid-portion of penile corpus; IIEF-5 – International Index of Erectile Function; kPa – kilo Pascal

to the development of ED. To our knowledge, although there are many studies about the causes of ED in COPD in the literature, the use, and effectiveness of SWE, a diagnostic method that can prove this, have never been questioned. Our study showed the effects of systemic inflammation caused by chronic hypoxia on the CC in patients with COPD who were evaluated as having good health status. Furthermore, our study supports that SWE is a promising method that can be used in the diagnosis of ED.

The exact mechanism of ED in males with COPD is not fully known. Multifactorial (hormonal, vascular, and psychological) mechanisms are thought to affect the emergence of this condition [16]. Karadag et al. reported that hypoxia in patients with COPD led to low testosterone levels. They also found that hormonal changes did not correlate with the ED score, and it was thought that hypoxia caused ED by causing systemic inflammation [17]. Furthermore, it was found that the levels of proinflammatory cyto-

kines including tumor necrosis factor (TNF)- α , interleukin (IL)-12, interferon (IFN)- γ , IL-1 β and IL-6, and transforming growth factor- β 1 (TGF- β 1), which is a cytokine with multiple functions, were higher in patients with COPD than in the normal population [18]. In addition, in cases of chronic hypoxia such as in COPD, there is an increase in TGF- β 1 concentration and decrease in prostaglandin E [17, 19, 20].

TGF- β 1 is a fibrogenic cytokine that is found in the CC in western blot analyses. Prostaglandin E is an autacoid agent that inhibits connective tissue synthesis and provides a balance between the connective tissue (collagen) and smooth muscle rate in the penis. TGF- β 1 changes the extracellular matrix structure around the cells by increasing the expression of collagen, fibronectin, and proteoglycan, and by inhibiting collagenase and other proteases. This change, especially in hypoxia, leads to an increase in TGF- β 1 and decrease in prostaglandin E concentrations, resulting in an increased accumulation of connective tissue and smooth muscle (SMC) atrophy in CC of the penis [20, 21].

In studies, the ratio of trabecular smooth muscle to all erectile tissue was reported to be related with erectile function [21]. A decrease of the ratio of smooth muscle in the penis below 30% impairs cavernosal blood flow and causes veno-occlusion, which lead to severe ED [20]. In their study conducted on animals, Zhang et al. revealed that the reduced amount of SMC was associated with higher results in SWE, and SWE could quantitatively show the amount of SMC [22]. In our study, the increase in SWE value and the decrease in IIEF-5 as COPD duration increased indicates that COPD's effect on CC paves the way for ED, and this is consistent with current studies.

The place of radiology in ED is limited; it is only used for diagnosis and treatment guidance in selected patients. In order to determine vascular pathologies, Doppler sonography, where intracavernosal vasodilator agents are administered, is frequently used [23]. But, intracavernosal injection has side effects such as penile pain, hematoma, and prolonged erection [24]. In addition, cavernosography and angiography, which are gold-standard diagnostic methods, are highly invasive methods [23]. SWE comes to the forefront as a noninvasive, fast, and practical method. However, SWE is a new method in the literature and therefore there are limited studies on its use in patients with ED and no clear cut-off values for penile tissue have been shown. This leads to the occurrence of variable results in different studies. In contradistinction to our research results, Türkay et al. detected SWE value as significantly low in patients with ED compared to the control group (20.94 ± 6.23 and 24.63 ± 7.58 , $p = 0.027$, respectively) [23]. In their study, the rate of the patients with psychogenic ED in the ED group was unclear, and this may have affected the research findings. On the contrary, Illiano et al. determined that SWE was negatively correlated with IIEF-5 and erection hardness score [25]. The findings of our study are consistent with the study of Illiano et al.

After developing irreversible cavernosal blood flow and veno-occlusion disorders, we can evaluate the pathology of the cavernosal hemodynamics by using parameters such as peak-systolic velocities, end-diastolic velocities, and resistance index in spectral Doppler ultrasonography [26]. However, although these parameters give us information about the vascular status of the penis, they cannot provide any information about tissue characteristics such as increased collagen in the penis and the smooth muscle status of penis, which can be seen in various phases of COPD. Evaluation of the changes in the penile tissue structure may be important in determining the treatment of ED and predicting the success rates of these treatment methods. The findings of our study support that SWE is a method that has a high potential in this respect. With further evidence, the use of SWE may have a place in the diagnosis, treatment plan, or follow-up of ED.

Our study has some limitations that should be taken into consideration. Although the data were collected prospectively, the patients were not randomized. This could have created selection bias. The results of our study were not confirmed by histopathologic evaluation, which prevented our findings from being clearer and more descriptive. The erection status of the patients was clearly assessed by clinical examination, but some participants did not provide objective information about penile health status. We believe that this situation could create a minor bias because we had to rely on the anamnesis of the patients. This was caused by the absence of an objective diagnostic tool for evaluating the erection status of the patients.

CONCLUSIONS

In our study, using data we gathered using SWE, we showed the effects of COPD on penile tissue and the effect of this on erectile function in patients. The correlation of our findings with the duration of COPD shows that the systemic adverse effects of chronic diseases that are not specific to the organ should always be taken into account. Although significant results were obtained in our study, clearer results will be reached in prospective randomized studies with more homogeneous patient groups with larger numbers of patients in the future.

CONFLICTS OF INTEREST

The authors declare that they have no conflicts of interest.

ETHICAL APPROVAL

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. The ethics committee of Dr. Sadi Konuk Training and Research Hospital approved this prospective study (Approval number: 2016/46).

INFORMED CONSENT

Informed consent was obtained from all individual participants included in the study.

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