HEALTH SCIENCES QUARTERLY

Volume: 2
Issue: 4
2022
E-ISSN: 2791-6022
https://journals.gen.tr/jsp

Received: 2022-03-06
Accepted: 2022-08-23

ORIGINAL ARTICLE

Thoracic computed tomography measures have predictive value in the diagnosis of chronic obstructive pulmonary disease

Mustafa Tosun[1] Edhem Ünver[1] Ali Küpeli[2]

Erdal Karavaş[3] Sonay Aydın[4]

1 Department of Chest Diseases, Faculty of Medicine, Erzincan Binali Yıldırım University. Erzincan / Türkiye
2 Department of Radiology, Trabzon Kanuni Training and Research Hospital. Trabzon / Türkiye
3 Department of Radiology, Faculty of Medicine, Bandırma Onyedi Eylül University. Balıkesir / Türkiye
4 Department of Radiology, Faculty of Medicine, Erzincan Binali Yıldırım University. Erzincan / Türkiye

Abstract

Chronic Obstructive Pulmonary Disease (COPD) is diagnosed with pulmonary function tests (PFTs). However, since not all patients can be diagnosed with PFTs, some are diagnosed with radiological or clinical findings. The purpose of this study was to define the properties of obstructive airway disease through thoracic computed tomography (CT) and to identify the diagnostic efficacy of CT findings. A total of 160 patients who underwent PFT and thoracic CT assessment July 2018 - January 2019, were retrospectively analyzed. Based on PFT findings, patients were categorized into three groups as having normal, restrictive or obstructive airways. Age, height, weight, and body mass indexes of the groups were recorded. Pulmonary height, width, right-left hemi-diaphragm height, sterno-diaphragmatic angle and retrosternal transparent area length in axial sections were also recorded. Diagnostic efficacies of these parameters in the detection of obstructive airway disease were measured. Of the 160 patients (109 males, 51 females; mean age = 59.5), 91 (56.9) had normal PFT, 58 (36.2%) had obstructive and 11 (6.9%) had restrictive airway disease. Pulmonary height, width, sterno-diaphragmatic angle, and retrosternal transparent area length were significantly higher in patients with obstructive airway disease while the right-left hemi-diaphragm height was significantly lower (p<0.001). About 60-75% sensitivity and specificity were obtained when identifying the obstructive airway disease with these parameters. These values obtained from the axial and sagittal sections could contribute to the diagnosis of obstructive airway disease.

Keywords: Chronic obstructive pulmonary disease, diagnosis, thorax computed tomography measurements, emphysema

Citation: Tosun M, Ünver E, Küpeli A, Karavaş E, Aydın S. Thoracic computed tomography measures have predictive value in the diagnosis of chronic obstructive pulmonary disease. Health Sci Q. 2022;2(4):187-96. https://doi.org/10.26900/hsq.2.4.03

Corresponding Author:
Erdal Karavaş
Email: erdalkaravas@hotmail.com

Introduction

Chronic Obstructive Pulmonary Disease (COPD) is a common preventable and treatable disease characterized with airflow restriction and respiratory symptoms arising from airways and/or alveolar anomalies generally induced by serious exposure to harmful particles or gases [1]. COPD is a leading cause of morbidity and mortality worldwide. Its prevalence has increased over years with the increasing exposure to risk factors and the ageing of population [2]. Although findings of COPD is deemed to be irreversible, it has been shown that progression of the disease can be prevented and health outcomes could be improved with early diagnosis.

Presence of symptoms is not always essential for the diagnosis of COPD. Rather, it is important to show exposure to risk factors and airflow restriction with pulmonary function testing (PFT). While chest radiography is the initial radiological inspection in the assessment of patients, it has low specificity and sensitivity values in the diagnosis of COPD (particularly in emphysema) [3].

Today, exposure to radiation has decreased with shortened duration of radiological examinations and it has become easier to assess the prevalence and anatomic distribution of parenchyma, particularly with thoracic computed tomography (CT) [4].

The relationship between the diagnosis of COPD and thoracic CT findings that include air trapping, bronchial wall thickness, tree-in-bud appearance, and thoracic cage ratios, has been identified in several research [5–9]. In this study,

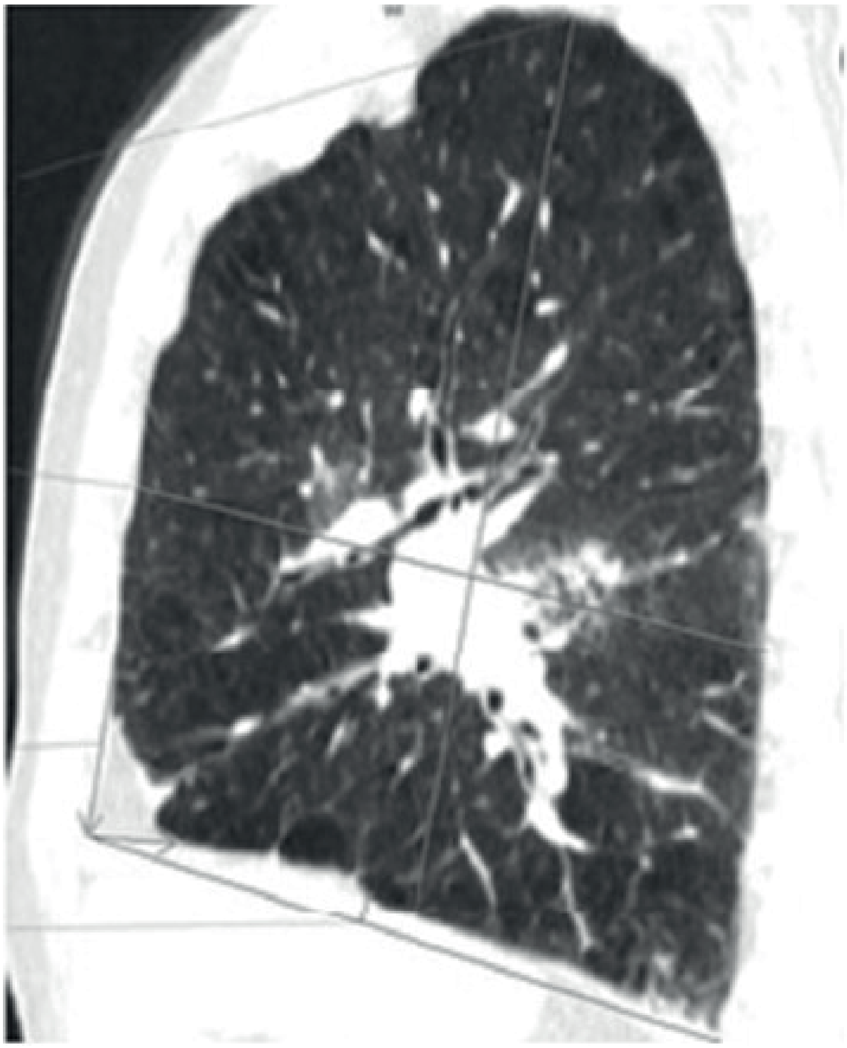

Figure 1. Measurements of pulmonary height, width, right-left hemi-diaphragm height, sterno-diaphragmatic angle in sagittal sections of thoracic CT of a patient with COPD.

we compared the thoracic CT findings of patients with normal PFT compatible with obstruction in order to determine the diagnostic efficacy of CT in COPD.

Materials and Methods

The study protocol was approved by the local Ethics Committee for Clinical Research (2019/04-10).

A total of 160 patients who underwent PFT and thoracic CT July 2018 - January 2019 were assessed retrospectively. PFT values of the patients were evaluated based on the GOLD guide to categorize the patients in 3 groups as having normal, restrictive or obstructive airways. Age, height, weight, and body mass index (BMI) of the groups were recorded.

Acquiring Thoracic CT images:

Images of the patients were acquired with the 16-detector Siemens SOMATOM Sensation 16 (Forchheim, Germany) CT device used in the Radiology Unit *(tube voltage= 120 kV, effective mAs = 90, slice thickness 5 mm, collimation = 2×4 mm, pitch = 1.6).*

Analysing the images:

The measures were taken with Syngo (Siemens Medical Solutions) software at workstation in thoracic CT inspections without notice of PFT

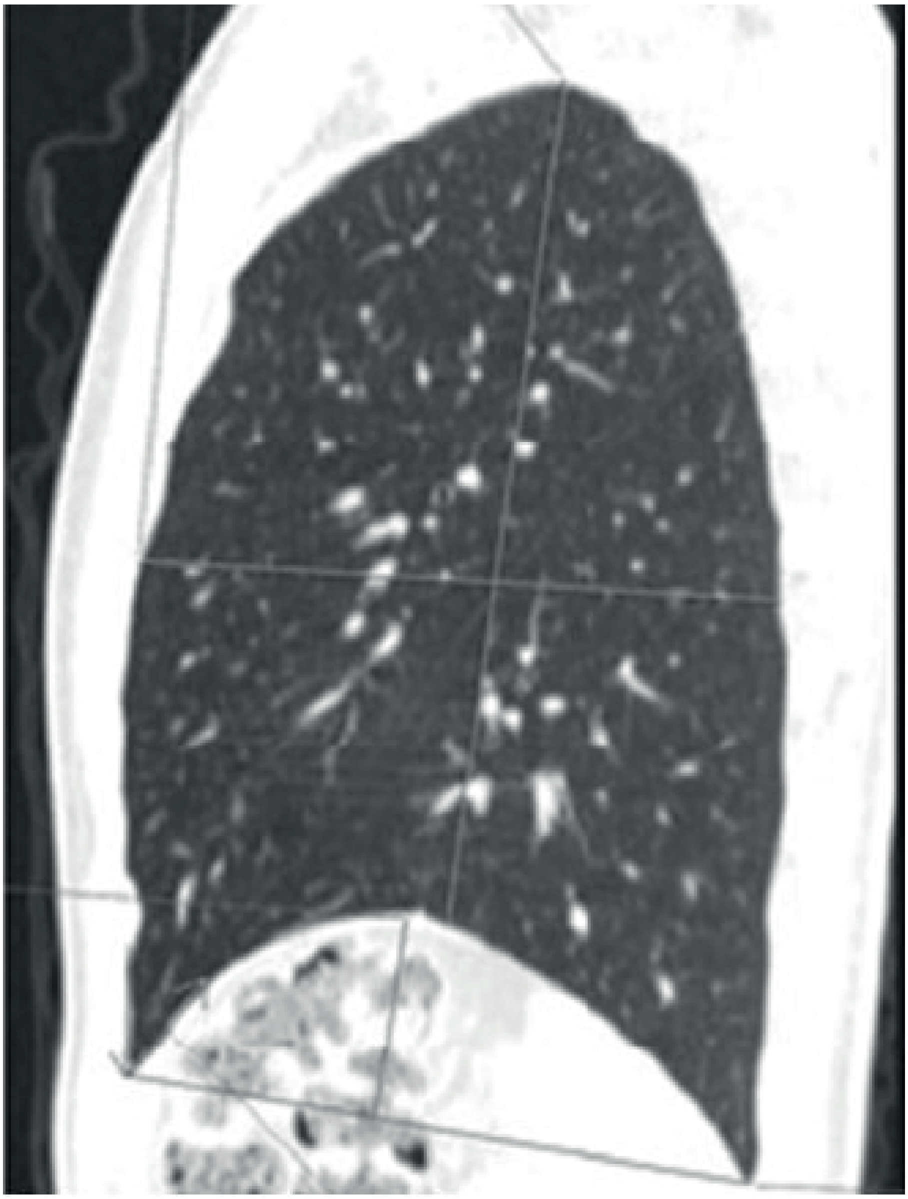

Figure 2. Measurements of pulmonary height, width, right-left hemi-diaphragm height, sterno-diaphragmatic angle in sagittal sections of thoracic CT of a person without COPD.

values upon the consensus of two radiologists with a minimum 5-year experience in the profession.

In sagittal sections;

1. Pulmonary height

2. Pulmonary width

3. Right-left hemi-diaphragm height

4. Stero-diaphragmatic angle measurements were performed (Figure 1,2).

In axial sections, retro-sternal transparent area length was recorded (Figure 3).

Patients with normal PFT testing findings and restrictive pattern and patients with obstructive pattern were compared in terms of these parameters in order to find out their diagnostic efficacy in the detection of obstructive airway disease. Mediastinum and parenchymal windows of the patients were also analyzed to see whether emphysema, bronchiectasis, peribronchial thickening, mucus seal and air trapping were present and the findings were recorded.

Results

Of the 160 patients included in the study, 109 were male and 51 were female. 91 (56.9%) had normal PFT, 58 (36.2%) had obstructive and 11 (6.9%) had restrictive airway disease. Comparison of the demographical data of the patients revealed that the mean age of the patients who had obstructive type of disease was significantly higher than the patients who didn't have such disease (p<0.001). BMI was also significantly higher in the obstructive group compared to the non-obstructive group (p=0.014). There was no significant difference in other demographical data (Table 1).

Compared to the patients with normal and restrictive PFT findings, the group with an obstructive airway disease had significantly higher mean values pulmonary height, width, sterno diaphragmatic angle, and retrosternal transparent area length while the group's mean right-left hemidiaphragm height was statistically significantly lower (p<0.001, Table 2).

About 60-75% sensitivity and specificity were obtained when identifying the obstructive

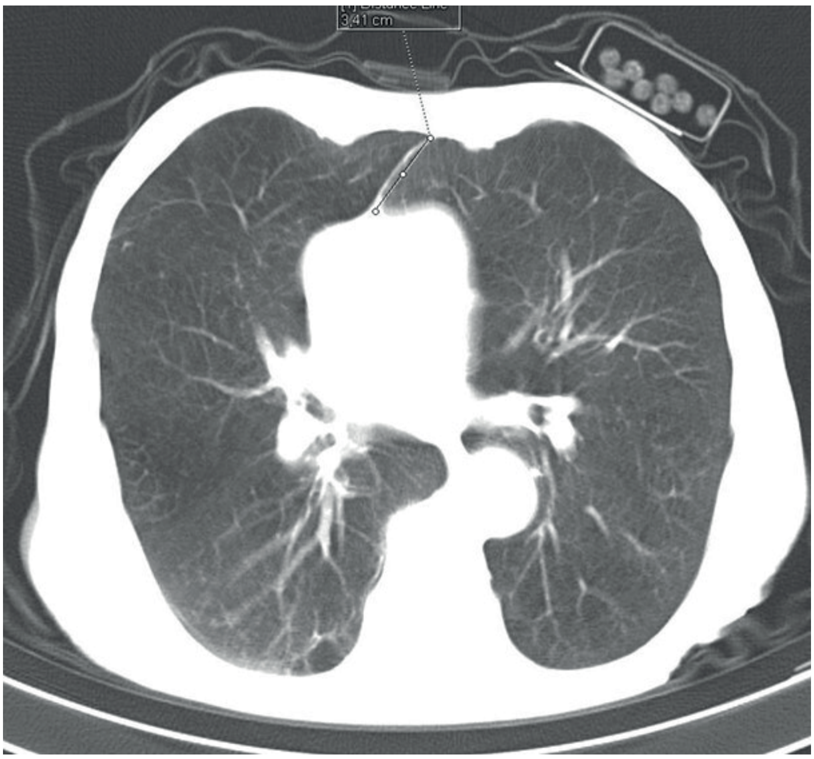

Figure 3. Retro-sternal transparent area length measurement in axial section.

airway disease with these parameters.

Parenchymal and mediastinal analysis revealed emphysema in 33 patients (20.6%). 22 of these patients were in the obstructive group (*p*<0.001). Among other findings, bronchiectasis was found in 21 patients (13.1%). 14 of these patients were in the obstructive group (*p*=0.002). Similar to emphysema, the ratio of patients diagnosed with peribronchial thickening (31.3%), air trapping (40%) and mucus seal (15%) was significantly higher in the obstructive group (*p*<0.001, Table 3).

While the highest sensitivity was found with pulmonary height (74.1%) and pulmonary width in ROC (Receiver Operating Characteristic) analysis, the highest specificity was found with the right hemidiaphragm height with a rate of 67.6%. Positive predictive values (PPV) of the findings were close to each other with a mean rate of 53%. When negative predictive values (NPV) were studied, they were measured around 80% in all findings, with the left hemidiaphragm had the highest value (81.9%). Besides, under the curve areas of these parameters, i.e. AUC values were between 0.690-0.739 and comparison of AUCs did not reveal any statistically significant difference (*p*=0.241). All ROC analysis findings are shown in Figure 4 and Table 4.

Table 1. Demographical features of the patients.

	Total	Obstructive Airway Disease		*p* value
		Yes	No	
Number	160	58	102	
Age	50.4 ± 14 (23-90)	64.3 ± 9 (44-88)	56.7 ± 14 (31-87)	<0.001
Sex Male				<0.002
Male	109	48	61	
Female	51	10	41	
Height (cm)	167.4 ± 8.7 (150-195)	163.8 ± 7.6 (145-178)	162.4 ± 10.4 (137–192)	0.397
Weight (kg)	83.4 ± 11.9 (53-140)	75.0 ± 15.1 (64.5-108)	79.9 ± 16.9 (51-137)	0.067
BMI	29.5 ± 6.2 (18.9–55.68)	30.4+ 6.6 (18.9-55.8)	27.9 ± 52 (19.2-44.3)	0.014

Abbreviations: BMI = Body mass index.

Table 2. Comparison of the parameters measured with thoracic CT.

	Total	Obstructive Airway Disease		*p* value
		Yes	No	
Number	160	58	102	
Pulmonary height	19.6 ± 2.9 (11.7-26)	21 ± 26 (13.7-26)	18.8 ± 2.8 (11.7-23.8)	<0.001
Pulmonary width	18.3 ± 19 (14.5-23.7)	19.4 ± 1.8 (14.5-23.7)	17.7 ± 1.7 (14.7-23)	<0.001
R hemi. height	37 ± 12.2 (8-71)	30.6 ± 14.1 (8-67)	40.7 ± 9.2 (19-71)	<0.001
L hemi height	31 ± 11.3 (7-67)	25 ± 11.9 (7-57)	34.5 ± 9.4 (11-67)	<0.001
R sterno. angle	63.2 ± 16.6 (26-169)	68.8 ± 15.5 (26-96)	60 ± 16.4 (30-169)	0.001
L sterno. angle	68.3 ± 16.9 (28-145)	74.3 ± 16.8 (28-96)	64.9 ± 16.1 (31-145)	0.001
R sterno. angle	10.6 ± 6.7 (4-46)	14.9 ± 8.3 (4-46)	8.1 ± 3.3 (4-20)	<0.001

Abbreviations: Hemi = hemidiaphragm; sterno= sterno-diaphragmatic.

Discussion

COPD is a leading health issue in terms of mortality, morbidity, and economic losses today. While investigation of new drugs and methods for the treatment of the disease continues, methods to be used in early diagnosis of the disease are under development. Early diagnosis and treatment are two major factors affecting the prognosis of the disease [2,3]. Being non-invasive, inexpensive and easily applicable in monitoring of the treatment, pulmonary function tests (PFTs) are among the main methods used in the diagnosis of COPD. So, they are primarily preferred in the phasing of the disease [3]. While

Table 3. Comparison of the findings obtained from the mediastinum and parenchymal window images of the patients.

	Total	Obstructive Airway Disease		*p* value
		Yes	No	
Emphysema				<0.001
Yes	33	22	11	
No	127	36	91	
Bronchiectasis				0.002
Yes	21	14	7	
No	139	44	95	
Peribronchial Thick.				<0.001
Yes	50	30	20	
No	110	28	82	
Air Trapping				< 0.001
Yes	64	37	27	
No	96	19	75	
Mucus Seal				<0.001
Yes	24	20	4	
No	136	38	98	

Abbreviations: Thick = thickening.

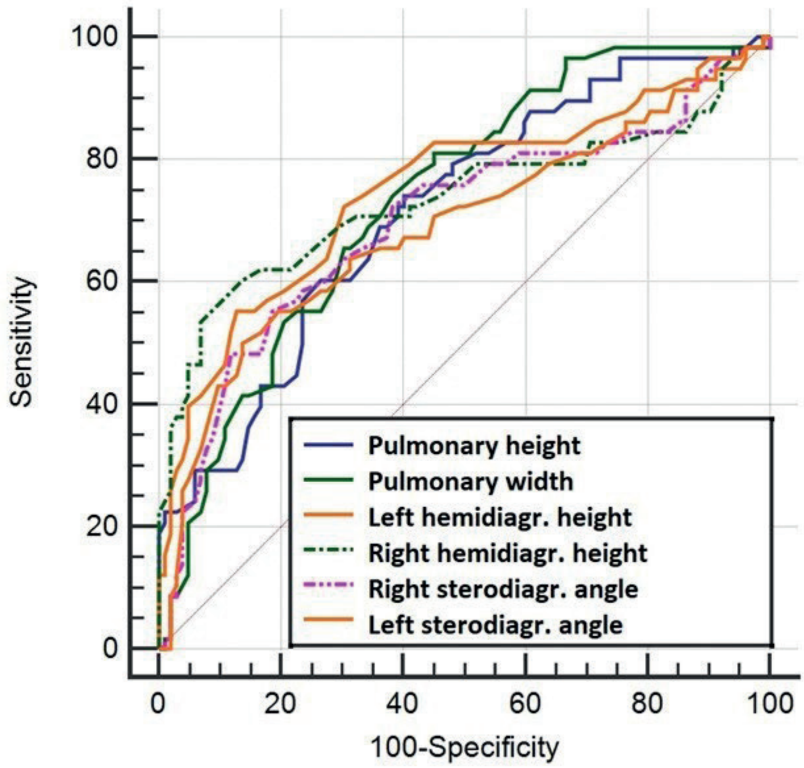

Figure 4. ROC analysis graphics.

PFT is deemed to be the gold standard, it has been suggested in a study that its rate of accuracy in the detection of the disease is between 62-64% when PFT values are considered together with clinical findings according to ATS and ERS guidelines [10]. While chest radiography is significant in the detection of additional parenchymal pathologies such as pneumonia, solitary pulmonary nodule, and pulmonary embolism, it is a method with low specificity and sensitivity in the diagnosis of COPD (particularly in emphysema) [11]. However, chest radiography will be a useful and primarily preferred method particularly in the differential diagnosis of COPD exacerbation, heart failure or acute pathologies like pneumothorax [12]. Vascular changes and hyperinflation are the most important indicators in chest radiography. The most radiologically reliable indicator of hyperinflation is the flattening of the diaphragm. This finding is also correlated with the degree of narrowing in airways [13,14].

Retro-sternal area above 2.5 cm, a pulmonary height >30 cm, long and narrow heart shape and enlarged costophrenic angle also support the presence of emphysema [15]. Despite all these, chest radiography is basically a method supporting diagnosis rather than being a diagnostic method. Thoracic CT is a method that is much more sensitive and specific than standard chest radiography [16–18]. Two basic methods as the visual method and quantitative assessment are used for the diagnosis of emphysema in CT. Correlation between visual assessment and histopathological assessment of emphysema has been shown by several studies in previous years [19–21]. There are also studies in which the detection of emphysema by quantitative CT is associated with PFT [22,23].

Sakai et al., carried out a study based on these criteria, where they used the observation method based on the prevalence and severity of emphysema and showed that there was a strong correlation between visual scoring values and PFT [24]. However, visual assessment has some disadvantages like subjectivity and the effects of observer's experience and different window settings on interpretation [25]. Thoracic CT and quantitative assessment are in parallel with technological developments. In a study conducted by Nakano et al. on 114 smokers, it was showed that there was a correlation between the right lung upper lobe segment bronchial diameter thickness and the narrowing in airways

Table 4. ROC analysis findings.

	AUC	Threshold Value	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)
Pulmonary height	0.717	19.6	74.1	59.8	51.2	80.3
Pulmonary width	0.736	18.3	74.1	61.7	52.4	80.8
R hemi. height	0.735	36	70.6	67.6	55.2	80.2
L hemi. height	0.749	31	74.1	66.6	55.8	81.9
R sterno. angle	0.699	62	72.4	61.7	51.9	79.9
L sterno. angle	0.690	69	65.5	63.7	50.7	76.5
Retro-sternal transparent a.	0.739	8	68.9	64.7	52.6	78.6

Abbreviations: Hemi = hemidiaphragm; sterno = sterno-diaphragmatic; a = area.

[26]. In another study, by examining thoracic CT scans taken for lung cancer screening, patients were evaluated for COPD and concluded that inspiratory thoracic CT biomarkers alone may be sufficient to identify patients with COPD [18].

In a study conducted by Hightower et al., PFT-diagnosed obstruction was found to be significantly correlated with sterno diaphragmatic angle and hemidiaphragm assessment among the quantitative assessments [27]. In the same study comparing the qualitative and quantitative measurements with regards to their demonstration of the presence of obstruction, specificity of qualitative measurements was over 90% while it changed between 80-90% in quantitative measurements. On the other hand, sensitivity was not high in either measurement [27]. Unlike that study, we found that pulmonary height and pulmonary width had the highest sensitivity with a rate of 74.1%, and right hemidiaphragm height had the highest specificity with a rate of 67.6%.

Mild and moderate emphysema cases are relatively asymptomatic. There is a mild difficulty in breathing in these patients yet coughing and phlegm are less than chronic bronchitis. Therefore, patients underestimate these symptoms and most of them spend many years without presenting to a hospital. Hence, early diagnosis rate of the disease decreases [24,28,29]. PFT cannot directly reveal emphysema when measuring pulmonary volumes, flow rates and the severity of obstruction. While many parameters in PFT reflect airway obstruction, they cannot show the parenchymal loss caused by emphysema. PFT can even display normal findings in the presence of the disease [24,30]. In a study evaluating the contribution of emphysema, air trapping and airway wall thickness measured by CT to lung functions, it was determined that each measurement contributed to a different PFT parameter [31]. In our study, thoracic CT findings of 33 of the 160 patients revealed emphysema. PFT of 2/3 of these 33 patients were obstructive (p<0.001). However, there were 11 more patients with normal PFT yet emphysema in thoracic CT. This showed that we could use thoracic CT to reveal the presence of emphysema in patients prior to the disruption of values in PFT. Indeed, thoracic CT has been reported to be the most effective method in the diagnosis of emphysema [22,32,33]. In a study conducted by Lakadamyali et al., patients underwent high resolution computed tomography (HRCT) to find out whether emphysema as a finding of COPD was present or not; and findings such as bronchiectasis, peribronchial thickening, air trapping and mucus seal were not included in the study [12]. In our study, all above-mentioned findings including emphysema were found to be significantly higher in the obstructive group.

Conclusion

In conclusion, early diagnosis and treatment of COPD is important for the reduction of mortality, morbidity, and treatment expenses. As obstructive changes do not occur in early stage in PFT, thoracic CT assessment of patients with suspected clinical findings could be helpful in early diagnosis. Although the high cost of PFT makes it difficult to be requested for each patient, we consider it to be advantageous in the reduction of annual loss of FEV1 as the diagnosed person will quit smoking and receive treatment. PFT could also be helpful in the detection of other findings that might be added to COPD.

Limitations: The main limitations of our study are its retrospective nature and the relatively small number of patients. In addition, although HRCT was generally used in previous similar studies, we used thorax CT and we did not take inspiration-expiratory measurements.

Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors

Conflict of interest

The authors declare that they have no conflict of interest.

References

1. Patel AR, Patel AR, Singh S, Singh S, Khawaja I. Global initiative for chronic obstructive lung disease: The changes made. Cureus. 2019;11(6):e4985. doi: 10.7759/cureus.4985.
2. Rosenberg SR, Kalhan R, Mannino DM. Epidemiology of chronic obstructive pulmonary disease: Prevalence, morbidity, mortality, and risk factors. Semin Respir Crit Care Med. 2015;36(4):457–69. doi:10.1055/s-0035-1555607.
3. 2021 GOLD Reports - Global Initiative for Chronic Obstructive Lung Disease - GOLD. Accessed September 28, 2021. https://goldcopd.org/2021-gold-reports.
4. Messerli M, Ottilinger T, Warschkow R, Leschka S, Alkadhi H, Wildermuth S, et al. Emphysema quantification and lung volumetry in chest X-ray equivalent ultralow dose CT - Intra-individual comparison with standard dose CT. Eur J Radiol. 2017;91:1-9. doi: 10.1016/j.ejrad.2017.03.003.
5. Webb WR. Radiology of obstructive pulmonary disease. Am J Roentgenol. 1997;169(3):637–47. doi:10.2214/ajr.169.3.9275869.
6. Arakawa H, Kurihara Y, Nakajima Y, Niimi H, Ishikawa T, Tokuda M. Computed tomography measurements of overinflation in chronic obstructive pulmonary disease: Evaluation of various radiographic signs. J Thorac Imaging. 1998;13(3):188-92.doi:10.1097/00005382-199807000-00005.
7. Takasugi JE, Godwin JD. Radiology of chronic obstructive pulmonary disease. Radiol Clin North Am. 1998;36(1):29–55. doi:10.1016/S0033-8389(05)70006-3.
8. Kasai T, Yamada M, Narushima M, Suzuki H. [Relationship between thoracic cross-sectional area measured on CT and pulmonary function or dyspnea in patients with COPD]. Nihon Kokyuki Gakkai Zasshi. 2003;41(8):526–30.
9. Rizzo A, Mulshine JL. Thoracic CT screening: Using routinely detectable COPD information. Clin Imaging. 2021;78:310-2. doi:10.1016/j.clinimag.2021.04.019.
10. Viegi G, Pedreschi M, Pistelli F, Di Pede F, Baldacci S, Carrozzi L, et al. Prevalence of airways obstruction in a general population: European Respiratory Society vs American Thoracic Society definition. Chest. 2000 ;117(5 Suppl 2):339-45. doi: 10.1378/chest.117.5_suppl_2.339s.
11. den Harder AM, Snoek AM, Leiner T, Suyker WJ, de Heer LM, Budde RPJ, et al. Can routine chest radiography be used to diagnose mild COPD? A nested case-control study. Eur J Radiol Eur J Radiol. 2017;92:159-65. doi: 10.1016/j.ejrad.2017.05.007.
12. Lakadamyalı H, Alpar S, Lakadamyalı H, Ertürk H, Kurt B. Kronik obstrüktif akciğer hastalığında yüksek rezolüsyonlu bilgisayarlı tomografi bulguları ile solunum fonksiyon testleri arasındaki korelasyon. Türk Toraks Dergisi. 2006;7(1):17-22.
13. Nicklaus TM, Stowell DW, Christiansen WR, Renzetti AD. The accuracy of the roentgenologic diagnosis of chronic pulmonary emphysema. Am Rev Respir Dis. 1966;93(6):889–99. doi:10.1097/00004424-196711000-00004.
14. Reich SB, Weinshelbaum A, Yee J. Correlation of radiographic measurements and pulmonary function tests in chronic obstructive pulmonary disease. Am J Roentgenol. 1985;144(4):695–9. doi:10.2214/ajr.144.4.695.
15. Greene R. “Saber sheath” trachea: Relation to chronic obstructive pulmonary disease. Am J Roentgenol. 1978;130(3):441–5. doi:10.2214/ajr.130.3.441.
16. Pauwels R, Buist S, Calverley P, Jenkins C, Hurd S. Global strategy for the diagnosis, management and prevention of chronic obstructive pulmonary disease. NHBLI/WHO global initiative for Chronic Obstructive Lung Disease (GOLD) workshop summary. Rev Port Pneumol. 2001;7(4–5):398–400. doi:10.1016/S0873-2159(15)30846-1.
17. De Torres JP, Bastarrika G, Wisnivesky JP, Alcaide AB, Campo A, Seijo LM, et al. Assessing the relationship between lung cancer risk and emphysema detected on low-dose CT of the chest. Chest. 2007;132(6):1932–8. doi:10.1378/chest.07-1490.
18. Mets OM, Schmidt M, Buckens CF, Gondrie MJ, Isgum I, Oudkerk M, et al. Diagnosis of chronic obstructive pulmonary disease in lung cancer screening computed tomography scans: Independent contribution of emphysema, air trapping and bronchial wall thickening. Respir Res. 2013;14(1):59. doi: 10.1186/1465-9921-14-59.
19. Bergin C, Muller N, Nichols DM. The diagnosis of emphysema. A computer tomographic-pathologic correlation. Am Rev Respir Dis. 1986;133(4):541–6. doi:10.1164/arrd.1986.133.4.541.
20. Hruban RH, Meziane MA, Zerhouni EA, Khouri NF, Fishman EK, Wheeler PS, et al. High resolution computed tomography of inflation-fixed lungs. Pathologic-radiologic correlation of centrilobular emphysema. Am Rev Respir Dis. 1987;136(4):935–40. doi:10.1164/ajrccm/136.4.935.
21. Kuwano K, Matsuba K, Ikeda T, Murakami J, Araki A, Nishitani H, et al. The diagnosis of

mild emphysema. Correlation of computed tomography and pathology scores. Am Rev Respir Dis. 1990;141(1):169–78. doi:10.1164/ajrccm/141.1.169.

22. Konietzke P, Wielpütz MO, Wagner WL, Wuennemann F, Kauczor HU, Heussel CP, et al. Quantitative CT detects progression in COPD patients with severe emphysema in a 3-month interval. Eur Radiol. 2020;30(5):2502-12. doi: 10.1007/s00330-019-06577-y.

23. Schroeder JD, McKenzie AS, Zach JA, Wilson CG, Curran-Everett D, Stinson DS, et al. Relationships between airflow obstruction and quantitative CT measurements of emphysema, air trapping, and airways in subjects with and without chronic obstructive pulmonary disease. AJR Am J Roentgenol. 2013;201(3):W460-70. doi: 10.2214/AJR.12.10102.

24. Sakai F, Gamsu G, Im JG, Ray CS. Pulmonary function abnormalities in patients with CT-determined emphysema. J Comput Assist Tomogr. 1987;11(6):963–8. doi:10.1097/00004728-198711000-00007.

25. Morgan MDL. Detection and quantification of pulmonary emphysema by computed tomography: A window of opportunity. Thorax. 1992;47(12):1001–4. doi:10.1136/thx.47.12.1001.

26. Nakano Y, Muro S, Sakai H, Hirai T, Chin K, Tsukino M, et al. Computed tomographic measurements of airway dimensions and emphysema in smokers correlation with lung function. Am J Respir Crit Care Med. 2000;162(3 I):1102–8. doi:10.1164/ajrccm.162.3.9907120.

27. Hightower JS, Amadi C, Den E, Schmitt JE, Shah RM, Miller WT. Back to the future: Sagittal CT in the evaluation of COPD. Eur Radiol. 2016;26(8):2730–9. doi:10.1007/s00330-015-4094-4.

28. Han M, Steenrod A, Bacci E, Leidy N, Mannino D, Thomashow B, et al. Identifying patients with undiagnosed COPD in primary care settings: Insight from screening tools and epidemiologic studies. Chronic Obstr Pulm Dis. 2015;2(2):103-21. doi: 10.15326/jcopdf.2.2.2014.0152.

29. Lange P, Ahmed E, Lahmar ZM, Martinez FJ, Bourdin A. Natural history and mechanisms of COPD. Respirology. 2021;26(4):298-321. doi: 10.1111/resp.14007.

30. Gurney JW, Jones KK, Robbins RA, Gossman GL, Nelson KJ, Daughton D, et al. Regional distribution of emphysema: Correlation of high-resolution CT with pulmonary function tests in unselected smokers. Radiology. 1992;183(2):457–63. doi:10.1148/radiology.183.2.1561350.

31. Mohamed Hoesein FA, de Jong PA, Lammers JW, Mali WP, Mets OM, Schmidt M, et al. Contribution of CT quantified emphysema, air trapping and airway wall thickness on pulmonary function in male smokers with and without COPD. COPD. 2014;11(5):503-9. doi: 10.3109/15412555.2014.933952.

32. Hackx M, Bankier AA, Gevenois PA. Chronic obstructive pulmonary disease: CT quantification of airways disease. Radiology. 2012;265(1):34-48. doi: 10.1148/radiol.12111270.

33. Nambu A, Zach J, Schroeder J, Jin G, Kim SS, Kim YI, et al. Quantitative computed tomography measurements to evaluate airway disease in chronic obstructive pulmonary disease: Relationship to physiological measurements, clinical index and visual assessment of airway disease. Eur J Radiol. 2016;85(11):2144-51. doi: 10.1016/j.ejrad.2016.09.010.