



## Quantitative study of lung structure in COPD patients based on low-dose Karl iterative reconstruction

Kvantitativna studija strukture pluća kod obolelih od HOBP na osnovu niskodozne Karlove iterativne rekonstrukcije

<sup>1</sup>Yizhai Ye\*, <sup>1</sup>Juehui Li<sup>†</sup>, Weigen Wang\*, Jianhua He\*, Qi Yang<sup>‡</sup>

\*Ninghai First Hospital, Department of Radiology, Ningbo, Zhejiang Province, China;  
<sup>†</sup>Baoan District Hospital of Traditional Chinese Medicine, Department of Pulmonary Diseases/Respiratory and Critical Care Medicine, Shenzhen, China; <sup>‡</sup>The First Hospital of Jiaxing (Affiliated Hospital of Jiaxing University), Department of Respiratory, Jiaxing, Zhejiang Province, China

<sup>1</sup>The two authors contributed equally to this study

### Abstract

**Background/Aim.** Low-dose Karl iterative reconstruction (KIR) is a commonly used technique in medical imaging. An iterative algorithm reduces the dose of X-ray radiation while ensuring image quality, making it a safer and more convenient imaging method. The aim of the study was to analyze the assessment value of low-dose KIR for the lung structure of patients with chronic obstructive pulmonary disease (COPD). **Methods.** The study included a total of 135 COPD patients undergoing bronchoscopic biopsy from August 2022 to July 2023. Low-dose KIR was conducted. Two groups were formed according to the lung structure examined by bronchoscopic biopsy: an airway remodeling group and a non-airway remodeling group. The examination indicators of low-dose KIR were compared. Receiver operating characteristic curves were plotted to analyze the clinical value of low-dose KIR for assessing the lung structure. **Results.** According to the examination results of chest X-ray, airway remodeling was done in 85 out of 135 (62.96%) COPD patients. The sensitivities, specificities, and areas under the curves of computed tomography value, noise value, signal-to-noise ratio, and contrast-to-noise ratio were 0.976 vs. 0.965 vs. 0.953 vs. 0.980, 0.960 vs. 0.940 vs. 0.927 vs. 0.753, and 0.623 vs. 0.643 vs. 0.670 vs. 0.640, respectively. **Conclusion.** Low-dose KIR proved to be a very accurate and fast method for the quantitative study of lung structure in COPD patients.

### Key words:

airway remodeling; algorithms; tomography, x-ray computed; diagnostic techniques and procedures; pulmonary disease, chronic obstructive.

### Apstrakt

**Uvod/Cilj.** Karlova iterativna rekonstrukcija (KIR) niskom dozom je tehnika koja se često koristi u medicinskom snimanju. Iterativni algoritam smanjuje dozu rendgenskog zračenja istovremeno osiguravajući kvalitet slike, što ga čini sigurnijom i pogodnijom metodom snimanja. Cilj rada bio je da se analizira vrednost procene niskodozne KIR za strukturu pluća obolelih od hronične opstruktivne bolesti pluća (HOBP). **Metode.** Studijom je obuhvaćeno ukupno 135 obolelih od HOBP podvrgnutih bronhoskopskoj biopsiji od avgusta 2022. do jula 2023. godine. Sprovedena je niskodozna KIR. Formirane su dve grupe prema strukturi pluća ispitanih bronhoskopskom biopsijom: grupa za remodelovanje disajnih puteva i grupa bez remodelovanja disajnih puteva. Upoređeni su indikatori ispitivanja KIR niskim dozama. Za analizu kliničkog značaja niskodozne KIR u proceni strukture pluća korišćene su *receiver operating characteristic* krive. **Rezultati.** Prema rezultatima ispitivanja rendgenskog snimka grudnog koša, remodeliranje disajnih puteva urađeno je kod 85 od 135 (62,96%) obolelih od HOBP. Senzitivnost, specifičnost i površina ispod krive vrednosti kompjuterizovane tomografije, vrednosti šuma, odnosa signal-šum i odnosa kontrast-šum iznosile su 0,976 vs. 0,965 vs. 0,953 vs. 0,980, 0,960 vs. 0,940 vs. 0,927 vs. 0,753, i 0,623 vs. 0,643 vs. 0,670 vs. 0,640, redom. **Zaključak.** Niskodozna KIR se pokazala kao veoma precizna i brza metoda za kvantitativno proučavanje strukture pluća kod obolelih od HOBP.

### Ključne reči:

disajni putevi, remodeliranje; algoritmi; tomografija, kompjuterizovana, rendgenska; dijagnostičke tehnike i procedure; pluća, opstruktivna bolest, hronična.

## Introduction

Chronic obstructive pulmonary disease (COPD) is a common and devastating lung condition characterized by incomplete reversible airflow limitation<sup>1,2</sup>. The morbidity rate of COPD is very high globally<sup>3</sup>. The risk factors for COPD include smoking, air pollution, occupational exposure, etc. Structural changes in the lungs are an important part of the pathophysiological process of COPD<sup>4</sup>, including airway wall inflammation and mucus hypersecretion, airway remodeling (AR)-induced airway structural changes, and pulmonary emphysema-induced alveolar destruction.

AR in COPD patients is associated with disease severity<sup>5</sup>, which has a complex mechanism and causes great harm. Therefore, it is important to assess whether AR occurs in COPD patients in order to improve their quality of life and prognosis. In routine clinical practice, AR in COPD patients is assessed by lung function tests, high-resolution computed tomography (CT), bronchoscopy, and histopathological examination. Both early diagnosis and standardized treatment are essential for ameliorating the prognosis of COPD patients.

Low-dose Karl iterative reconstruction (KIR) is a commonly used technique in medical imaging. An iterative algorithm reduces the dose of X-ray radiation while ensuring image quality, making it a safer and more convenient imaging method.

The aim of this study was to assess the effect of low-dose KIR on the lung structure of COPD patients in order to explore its diagnostic value for structural changes.

## Methods

A total of 135 COPD patients undergoing bronchoscopic biopsy from August 2022 to July 2023 were recruited. Low-dose KIR was performed for all patients. There were 89 male and 46 female patients aged 56–84 years, with a mean age of  $70.39 \pm 13.82$  years. Among them, 63 patients had a smoking history, 55 had occupational exposure (harmful gases or dust in the work environment), and 39 had a family history (similar diseases in the family). Meanwhile, 62 cases were complicated with cardiovascular diseases, 71 had diabetes mellitus, and 59 had a history of cardiovascular disease. This study was approved by the local Ethics Committee, the First Hospital of Jiaying, Jiaying, Zhejiang Province, China (from August 6, 2022).

### *Inclusion and exclusion criteria*

Inclusion criteria were as follows: patients who met the diagnostic criteria for COPD in the Global Initiative for Chronic Obstructive Lung Disease Global Strategy for the Diagnosis, Management, and Prevention of Chronic Obstructive Pulmonary Disease 2018<sup>6</sup>, i.e., without any other diseases that may cause lung volume changes, such as chest deformity; those with forced expiratory volume in

1 second (FEV1)/forced vital capacity (FVC) – FEV1/FVC < 0.70 after inhalation of bronchodilators; those with very clear and complete dual-gas phase CT images of the chest and very clear images of the lung tissue; those who signed the informed consent form.

Exclusion criteria were as follows: patients with poor cooperation or blurred images; those with conditions that may affect the lung volume, including a history of lung surgery (such as lobectomy or segmentectomy) or morphological abnormalities of the chest; those with tumors or tumor-like lesions in the lungs; those with diseases that may affect CT scan results, such as infections in most of the lungs, severe atelectasis, or lung consolidation; those with more severe health problems, such as heart-, liver-, or kidney-related diseases.

### *Low-dose Karl iterative reconstruction*

The examination method and purpose were explained to the patients in detail before they signed the informed consent form. Prior to the examination, the patients were guided to receive breathing training until meeting the requirements in the scan, and they were instructed to hold their breath by command at the end of deep inspiration and deep expiration. CT scanner uCT-760 128-slice spiral (Shanghai United Imaging Healthcare Co., Ltd., China) was used.

The scanning conditions and parameters were as follows: for the routine dose – tube voltage of 120 kV, tube current of 150 mA, 40 mm collimation, pitch of 1.0875, 0.5 s/r, 5 mm slice thickness, 1-mm thin-slice reconstruction on inspiratory and expiratory phase images, field of view of 35 mm, and  $1024 \times 1024$  matrix; under a low dose – tube voltage of 120 kV, tube current of 80 mA, 40 mm collimation, pitch of 1.0875, 0.5 s/r, 5 mm slice thickness, 1-mm thin-slice reconstruction on inspiratory and expiratory phase images, field of view of 35 mm, and  $1024 \times 1024$  matrix.

The patient held the head with both hands facing forward in a supine position, and the whole lung was scanned after breath-holding at the end of deep inspiration and deep expiration. The scanning range was consistent.

### *Examination parameters of low-dose Karl iterative reconstruction*

All images were imported into the “digital lung” test platform for lobe segmentation and bronchus quantification. Lobe segmentation procedures are described in the text that follows. The whole lung tissue was extracted using the adaptive border marching method. Interlobular fissures were detected and segmented by computational geometry, and the implicit function method was used for segmenting a few interlobular fissures. Bronchus quantitative analysis software had been verified, automatically extracting the bronchial skeleton and measuring quantitative indicators required by the skeleton extraction algorithm when used for bronchus segmentation. To be specif-

ic, following lobe segmentation, the quantitative data, including the whole lung volume, volumes less than -910 Hounsfield units (HU) and -950 HU in both lungs, percentage of total lung area occupied by low attenuation area – LAA (LAA-950%, LAA-910%), emphysema index, and mean lung density, were measured. The quantitative indicators, including the number, length, and volume of bronchi, were obtained using the bronchus quantitative analysis software.

#### *Evaluation of airway remodeling in COPD patients undergoing bronchoscopic biopsy*

The airway wall thickness was measured to assess whether it was beyond the normal range. The morphology and arrangement of epithelial cells, as well as stromal changes, were observed. The collagen content and distribution were detected. The number and distribution of smooth muscle cells were observed. The type and number of inflammatory cells were assessed.

#### *Statistical analysis*

SPSS 26.0 software was used for statistical analysis. All measurement data were analyzed using the Shapiro-Wilk normality test. The normally distributed measurement data were described by mean  $\pm$  standard deviation and compared by the independent-samples *t*-

test between the two groups. Count data were described by percentages and analyzed using the Chi-square test. Receiver operating characteristic (ROC) curves were plotted to detect the clinical value of low-dose KIR for assessing the lung structure by the area under the curve (AUC):  $AUC \leq 0.50$  – no assessment value;  $0.50 < AUC \leq 0.70$  – low assessment value;  $0.70 < AUC \leq 0.90$  – medium assessment value;  $AUC > 0.90$  – high assessment value. The value of  $p < 0.05$  was considered statistically significant.

## Results

Bronchoscopic biopsy showed that AR occurred in 85 out of 135 (62.96%) COPD patients.

There was no significant difference in the general data between the two groups ( $p > 0.05$ ) (Table 1).

The AR group had significantly higher CT value, noise value, and signal-to-noise ratio, and a lower contrast-to-noise ratio than those of the non-AR group ( $p < 0.05$ ) (Table 2).

The ROC curves were plotted with the results of bronchoscopic biopsy as a state variable (presence of airway remodeling = 1, absence of airway remodeling = 0) and the criteria for objective evaluation of low-dose KIR image quality as a test variable (Figures 1 and 2). The results revealed that low-dose KIR had a high value for assessing lung structure in COPD patients (Table 3).

**Table 1**

**General data of patients with chronic obstructive pulmonary disease**

Variable	Pathological results by bronchoscopic biopsy		$t/\chi^2$	<i>p</i>
	AR Group (n = 85)	non-AR Group (n = 50)		
Age, years	71.32 $\pm$ 14.56	69.29 $\pm$ 9.89	0.874	0.384
Gender				
male	63	26	1.639	0.201
female	22	24		
Smoking history				
yes	41	22	0.052	0.821
no	44	28		
Occupational exposure				
yes	32	23	0.209	0.648
no	53	27		
Family history				
yes	15	24	3.559	0.059
no	70	26		
Complications with cardiovascular disease				
yes	35	27	0.477	0.490
no	50	23		
Complications with diabetes mellitus				
yes	46	25	0.049	0.825
no	39	25		
History of cardiovascular diseases				
yes	36	23	0.039	0.844
no	49	27		

Values are given as mean  $\pm$  standard deviation or numbers.

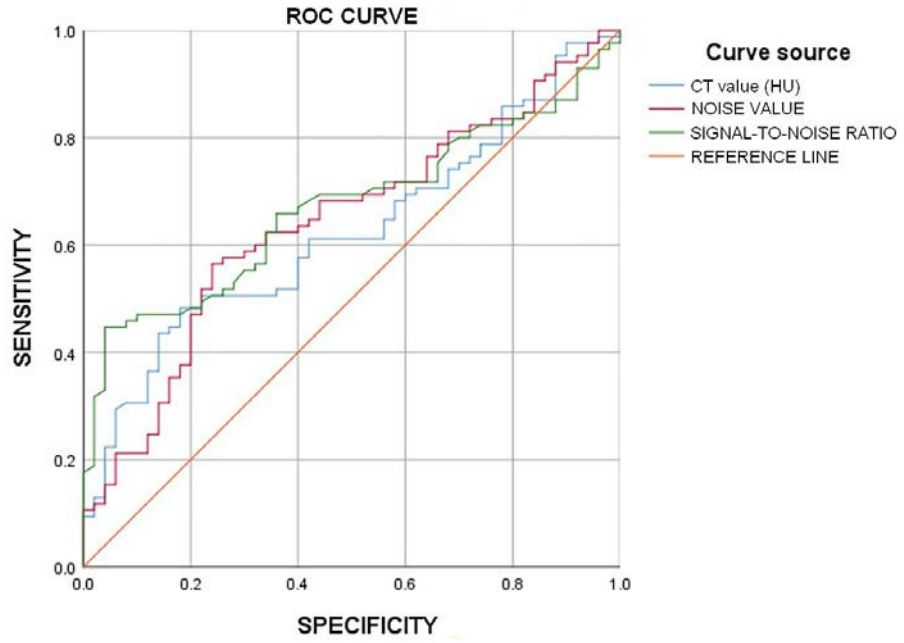
AR – airway remodeling.

**Table 2**

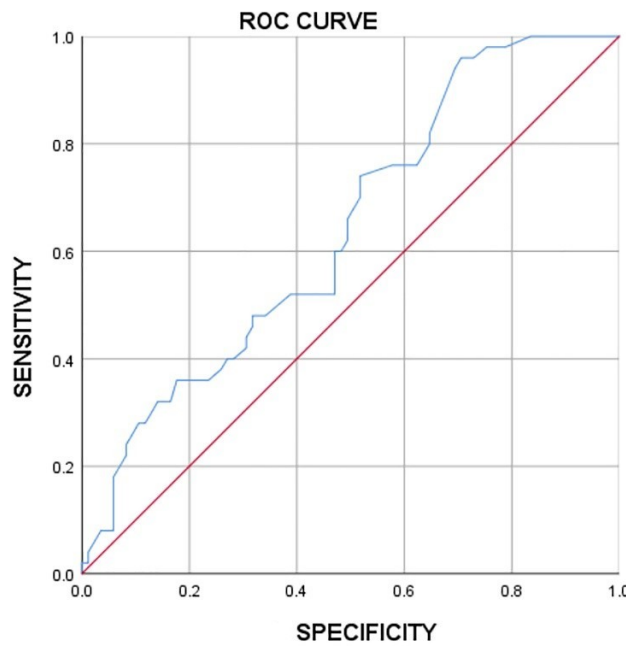
**Objective evaluation results of low-dose Karl iterative reconstruction image quality**

Lung structural changes in COPD	CT value (HU)	Noise	Signal-to-noise ratio	Contrast-to-noise ratio
Group				
AR (n = 85)	63.40 ± 9.36	37.61 ± 7.41	2.25 ± 0.80	0.32 ± 0.29
non-AR (n = 50)	59.46 ± 7.53	34.04 ± 6.60	1.82 ± 0.43	0.44 ± 0.30
<i>t</i>	2.532	2.812	3.510	2.292
<i>p</i>	0.013	0.006	0.001	0.024

COPD – chronic obstructive pulmonary disease; CT – computed tomography; AR – airway remodeling; HU – Hounsfield unit. Values are given as mean ± standard deviation.



**Fig. 1 – ROC curve analysis of low-dose Karl iterative reconstruction for assessing lung structural changes in COPD patients [CT value (HU), noise value, and signal-to-noise ratio].**  
 ROC – receiver operating characteristics. For other abbreviations, see Table 2.



**Fig. 2 – ROC curve analysis of low-dose Karl iterative reconstruction for assessing lung structural changes in COPD patients (contrast-to-noise ratio).**  
 ROC – receiver operating characteristics; COPD – chronic obstructive pulmonary disease.

**Table 3****Clinical value of low-dose Karl iterative reconstruction for assessing the lung structure in COPD patients**

Variable	Area under the curve	95% CI	<i>p</i>	Sensitivity	Specificity	Youden index
CT value (HU)	0.623	0.530–0.717	0.017	0.976	0.960	0.016
Noise value	0.643	0.548–0.737	0.006	0.965	0.940	0.025
Signal-to-noise ratio	0.670	0.581–0.760	0.001	0.953	0.927	0.026
Contrast-to-noise ratio	0.640	0.547–0.734	0.007	0.980	0.753	0.227

CI – confidence interval.

For other abbreviations, see Table 2.

### Discussion

With the aggravation of population aging, the morbidity rate of COPD has also been gradually increasing<sup>7</sup>. As the CT technique develops continuously, people have also had an increasing demand for routine CT examinations or diagnosis and determination of the severity of disease<sup>8</sup>. However, the damage of high radiation doses in CT to mental and physical health is inevitable. To address these problems, low-dose CT scans have been proposed to reduce the radiation dose<sup>9</sup>. Nevertheless, the image resolution declines and the image noise increases due to dose reduction, affecting the evaluation of the severity of disease and decision-making on the correct treatment. Iterative reconstruction has also been widely used, gradually becoming a new research hotspot. It is important to reduce the dose without compromising the image quality<sup>10</sup>.

Low-dose KIR is an image reconstruction algorithm with specific functions. Generally, it is applied in the quantitative study of the lung structure in COPD patients. It has been verified that the KIR algorithm can be used as a substitute for routine doses for diagnosing COPD, achieving similar diagnostic efficacy to the routine dose<sup>11</sup>.

In this study, the AR group had a higher CT value, noise value, and signal-to-noise ratio, and lower contrast-to-noise ratio than the non-AR group. Thus, low-dose KIR had a high value for assessing the lung structure in COPD patients. Moreover, the AUCs of CT value, noise value, signal-to-noise ratio, and contrast-to-noise ratio were 0.623, 0.643, 0.670, and 0.640, respectively, suggesting high diagnostic values for airway remodeling.

Low-dose KIR has many advantages in assessing the lung structure in COPD patients. For instance, compared with traditional CT, the radiation dose significantly declines, weakening the risks and potential hazards to the health of patients, especially those who need frequent CT examinations<sup>12, 13</sup>. The technique is also cost-effective, with shorter scanning time and fewer consumables due to decreased radiation dose<sup>14</sup>. In addition, surgeons and radiologists involved are safe against radiation exposure<sup>15</sup>. The low-dose KIR with a strong ability of lung structure detection in COPD patients can detect AR better by optimizing the image quality and reconstruction algorithm, thereby helping doctors assess the lung structure more accurately. Moreover, this technique also allows accurate quantitative analysis, which can provide more accurate parameters of lung structure to help assess disease progres-

sion and monitor the condition changes in COPD<sup>16, 17</sup>. Meanwhile, this technique can reduce image noise through the iterative reconstruction algorithm, and clear images can still be acquired at low doses, which is conducive to discovering subtle structural changes and displaying lung microstructure and lesion characteristics. Through regular examinations, doctors can also understand the changes in disease conditions to provide a basis for individualized treatment<sup>18</sup>.

The low-dose KIR is of great clinical significance for assessing the lung structure in COPD patients due to the following advantages<sup>19</sup>. Firstly, it can provide more detailed and accurate information about the lung structure, assist in early identification and diagnosis of COPD, provide a basis for individualized treatment by tracking disease progression and monitoring condition changes, guide treatment decision-making, determine the outcomes of therapeutic regimen, and help predict the prognosis. Secondly, it causes less radiation damage in order to reduce potential risks and improve safety. Thirdly, clearer images can be acquired with optimized image quality to facilitate diagnosis, provide a more reliable basis for doctors, and enhance diagnostic confidence. Finally, it can provide data support for related research, improve patient experience, and enhance medical quality<sup>20</sup>.

### Conclusion

Low-dose Karl iterative reconstruction has high value for assessing lung structure in COPD patients. This method not only quantitatively studies the lung structure in COPD patients but also determines the health of lung structure in COPD patients more comprehensively in combination with the actual condition of lung structure. Hence, more targeted treatment plans can be developed, the progression of disease predicted, and individualized suggestions for prevention and healthcare can be given to patients.

### Conflict of interest

The authors declare no conflict of interest.

### Funding

This study was financially supported by the Key Construction Disciplines of Provincial and Municipal Construction of Zhejiang Province (No. 2023-SSGJ-002).

## R E F E R E N C E S

1. *Christenson SA, Smith BM, Bajadhel M, Putcha N.* Chronic obstructive pulmonary disease. *Lancet* 2022; 399(10342): 2227–42.
2. *Ferrera MC, Labaki WW, Han MK.* Advances in Chronic Obstructive Pulmonary Disease. *Annu Rev Med* 2021; 72: 119–34.
3. *Yang LA, Jenkins CR, Sahi SS.* Chronic obstructive pulmonary disease in never-smokers: risk factors, pathogenesis, and implications for prevention and treatment. *Lancet Respir Med* 2022; 10(5): 497–511.
4. *Calverley PMA, Walker PP.* Contemporary Concise Review 2022: Chronic obstructive pulmonary disease. *Respirology* 2023; 28(5): 428–36.
5. *Upadhyay P, Wu CW, Pham A, Zeki AA, Royer CM, Kodavanti UP, et al.* Animal models and mechanisms of tobacco smoke-induced chronic obstructive pulmonary disease (COPD). *J Toxicol Environ Health B Crit Rev* 2023; 26(5): 275–305.
6. *Brassington K, Selemidis S, Bozinovski S, Vlahos R.* Chronic obstructive pulmonary disease and atherosclerosis: common mechanisms and novel therapeutics. *Clin Sci (Lond)* 2022; 136(6): 405–23.
7. *Long B, Rezaie SR.* Evaluation and Management of Asthma and Chronic Obstructive Pulmonary Disease Exacerbation in the Emergency Department. *Emerg Med Clin North Am* 2022; 40(3): 539–63.
8. *Adrish M, Anand MP, Hanania NA.* Phenotypes of Asthma-Chronic Obstructive Pulmonary Disease Overlap. *Immunol Allergy Clin North Am* 2022; 42(3): 645–55.
9. *Lee AHY, Snowden CP, Hopkinson NS, Pattinson KTS.* Pre-operative optimisation for chronic obstructive pulmonary disease: a narrative review. *Anaesthesia* 2021; 76(5): 681–94.
10. *Hanania NA, Boulet LP.* Asthma-Chronic Obstructive Pulmonary Disease: An Update. *Immunol Allergy Clin North Am* 2022; 42(3): xiii–xiv.
11. *Shao KM, Bernstein JA.* Asthma-Chronic Obstructive Pulmonary Disease Overlap: The Role for Allergy. *Immunol Allergy Clin North Am* 2022; 42(3): 591–600.
12. *Rhee CK.* Chronic obstructive pulmonary disease research by using big data. *Clin Respir J* 2021; 15(3): 257–63.
13. *Volpato E, Toniolo S, Pagnini F, Banfi P.* The Relationship Between Anxiety, Depression and Treatment Adherence in Chronic Obstructive Pulmonary Disease: A Systematic Review. *Int J Chron Obstruct Pulmon Dis* 2021; 16: 2001–21.
14. *Jeyachandran V, Hurst JR.* Advances in chronic obstructive pulmonary disease: management of exacerbations. *Br J Hosp Med (Lond)* 2022; 83(7): 1–7.
15. *Fuhlbrigge AL.* Epidemiology of Asthma-Chronic Obstructive Pulmonary Disease Overlap. *Immunol Allergy Clin North Am* 2022; 42(3): 533–47.
16. *Pellicori P, Cleland JGF, Clark AL.* Chronic Obstructive Pulmonary Disease and Heart Failure: A Breathless Conspiracy. *Cardiol Clin* 2022; 40(2): 171–82.
17. *Huo X, Jin S, Wang Y, Ma L.* DNA methylation in chronic obstructive pulmonary disease. *Epigenomics* 2021; 13(14): 1145–55.
18. *Sobala R, De Soyza A.* Bronchiectasis and Chronic Obstructive Pulmonary Disease Overlap Syndrome. *Clin Chest Med* 2022; 43(1): 61–70.
19. *Hurst JR, Han MK, Singh B, Sharma S, Kaur G, de Nigris E, et al.* Prognostic risk factors for moderate-to-severe exacerbations in patients with chronic obstructive pulmonary disease: a systematic literature review. *Respir Res* 2022; 23(1): 213.
20. *Wu F, Deng ZS, Tian HS, Li HQ, Zhou YM.* Progress in pre-chronic obstructive pulmonary disease. *Zhonghua Jie He He Hu Xi Za Zhi* 2023; 46(10): 1028–34. (Chinese)

Received on June 7, 2024

Revised on November 20, 2024

Accepted on November 27, 2024

Online First February, 2025