Supplemental Materials

The prevalence and physiological impacts of centrilobular and paraseptal emphysema on CT in smokers with Preserved Ratio Impaired Spirometry

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Supplemental Methods

Study subjects

This study retrospectively evaluated data of spirometry and full inspiratory chest CT. Non-smokers and smokers aged 40 years or older who underwent chest CT for lung cancer screening and spirometry without bronchodilator were consecutively enrolled at four facilities and the eligibility for the present analyses was assessed. The exclusion criteria were 1) a history of lung resection, 2) chest CT abnormalities extending to more than one lobe (such as consolidations, atelectasis, tumors, pneumothorax and thoracic deformity), 3) missing information on smoking status or light-smokers (< 10 pack-years), 4) more than 90 days between spirometry and CT scanning, and 5) insufficient inspiratory chest CT defined as $FVC>TLC_{CT}$. In the Tsukuba Medical Center, total 770 subjects underwent chest CT from November 2019 to September 2021. Nine subjects had abnormal CT findings or insufficient inspiratory CT, 155 subjects were missing demographic data, and 27 subjects were light-smoker. Ultimately, 579 subjects completed CT analyses. In the Kitano Hospital, total 356 subjects underwent chest CT for lung cancer screening from August 2012 to June 2014. Eleven subjects lacked demographic data, 13 subjects had abnormal CT findings or insufficient inspiratory CT, 4 subjects failed spirometry, and 30 were light-smokers. In the Takeda Hospital, total 885 subjects underwent chest CT from April 2016 to November 2020. Thirty subjects had abnormal CT findings or insufficient inspiratory chest CT, and 90 subjects were light-smokers. In the fourth facility (Terada Clinic, Respiratory Medicine and General Practice, Himeji), total 340 outpatients or subjects underwent chest CT for lung cancer screening from October 2018 to August 2020. Sixty-six subjects lacked demographic data, 41 subjects had abnormal CT findings or insufficient inspiratory CT, 42 subjects performed spirometry more than 90 days apart from chest CT scanning and 14 subjects were light-smokers.

Visual emphysema assessments

Six CT-experienced pulmonologists with at least 5-year experiences and a chest radiologist with 15-year experience performed visual emphysema analysis based on the Fleischner Society classification system [1]. CLE was classified as trace, mild, moderate, confluent or advanced destructive, while PSE was classified as mild or substantial [1]. The category of panlobular emphysema was not used in this study, as it is applied to patients with α1-antitrypsin deficiency [1]. Before assessing visual emphysema score in the study population, the analysts scored training CT datasets and substantial discordance was reviewed by the analysts to obtain consensus. Each CT scan was assessed by two analysts without knowledge of clinical information. When the assessment was disagreed among them, the final decisions was made by a chest radiologist. The images were viewed at window width 700 Hounsfield Unit and window level -750 Hounsfield Unit. The CT slice thickness was 0.5 to 1.25 mm. The weighted kappa coefficient was calculated for the severity of CLE and PSE. The severity of CLE (none/trace/mild/moderate/confluent/advanced destructive) was weighted from 0 to 5, and that of PSE (none/mild/substantial) was weighted from 0 to 2.

Reference

[1] Lynch DA, Austin JHM, Hogg JC, et al. CT-Definable Subtypes of Chronic Obstructive Pulmonary Disease: A Statement of the Fleischner Society. Radiology. 2015 Oct 11;277(1):192–205. doi: 10.1148/radiol.2015141579

Supplemental Table 1. Observer agreement for visual CT assessment

Observer	No. of chest CT scans	PSE agreement	Weighted kappa coefficient for PSE	CLE agreement	Weighted kappa coefficient for CLE
Observer 1 vs Observer 2	578	97.8 %	0.94	99.0 %	0.99
Observer 3 vs Observer 4	874	90.2 %	0.73	90.5 %	0.83
Observer 3 vs Observer 5	246	85.0 %	0.81	76.8 %	0.83
Observer 3 vs Observer 6	120	85.8 %	0.81	70.0 %	0.90

PSE = paraseptal emphysema, CLE = centrilobular emphysema

Supplemental Table 2. Subject's characteristics who underwent inspiratory and expiratory chest CT

No. of subjects	67
Age (years)	70.3 ± 11.4
No. of males*	56 (83.6%)
BMI (kg/m^2)	23.1 ± 4.3
Smoking status, current*	30 (44.8%)
Pack-years, ≥ 20 pack-year*	59 (88.1%)
FVC (predicted %)	82.1 ± 20.9
FEV_1 (predicted %)	72.0 ± 27.2
FEV_1/FVC	0.67 ± 0.14
TLC_{CT} (predicted %)	88.3 ± 13.8
FVC/TLC_{CT} (%)	54.9 ± 15.7
Lung function categories	
Normal spirometry*	18 (26.9%)
PRISm*	14 (20.9%)
Airflow limitation*	35 (52.2%)

Except where indicated, numbers are means ± standard deviations.
BMI = body mass index, FVC = forced vital capacity, FEV_1 = forced expiratory volume in 1 second, TLC_{CT} = total lung capacity measured on CT, FVC/TLC_{CT} = ratio of forced vital capacity to total lung capacity measured on CT, PRISm = preserved ratio impaired spirometry
*Data are numbers of subjects, with percentages in parentheses.

Supplemental Table 3. Correlation between FVC/TLC_{CT} and inspiratory-expiratory CT air-trapping indexes

Variables	Correlation coefficient	P value
Expiratory low attenuation volume (%)	-0.55	<0.01
Expiratory mean lung density (HU)	0.56	<0.01
Expiratory and inspiratory mean lung density ratio	-0.51	<0.01

Correlation between FVC/TLC_{CT} and other CT indexes were calculated with Pearson's correlation test. FVC/TLC_{CT} = ratio of forced vital capacity to total lung capacity measured on CT, HU = Hounsfield Unit