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Brief communication (Original)

CT features of normal lung change in asymptomatic elderly patients

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Background: Not all morphological lung changes in the elderly contribute to respiratory disease and may be a consequence of normal aging.
Objectives: To describe the changes in asymptomatic elderly patients compared with those in younger patients in a Thai population.
Methods: The study cohort comprised 60 participants without respiratory symptoms in three groups of 20 by age: 20–40 years, 41–60 years, and >60 years. Participants were prospectively selected from patients referred for computed tomography (CT) of the abdomen, or head and neck, and underwent sequential CT during deep breathing at four lung levels. Two observers scored images by consensus. We compared groups using Pearson chi-square and Fisher exact tests, and used receiver operating characteristic curves to categorize bronchiectasis and bronchial wall thickening by age.
Results: Air trapping was related to age (5/20 group 1, 7/20 group 2, and 18/20 group 3 (P <0.01)) and was most prevalent in lower lobes (78%, P < 0.01). Reticulation was found in only one middle aged patient (P = 0.36). Bronchiectasis was more common in patients <56 years (7/23) than <56 years (3/37), P = 0.035. Bronchial wall thickening (7/23 in patients >56 years and 2/37 in patients <56 years, P = 0.02) and extensive air trapping were related to age (0/6 group 1, 1/6 group 2, and 5/6 group 3, P = 0.02). Findings were independent of smoking history.
Conclusions: Asymptomatic older patients had higher prevalence of bronchiectasis, bronchial wall thickening, and air trapping, independent of smoking history.

Keywords: Aging lung, asymptomatic, CT, reticulation, senile lung

The population in Thailand is aging and life expectancy has been increasing. This creates an increased use of health care resources. Better understanding of the physiology and pathology of the elderly is needed to decrease unnecessary invasive investigations and avoid misdiagnosis of important diseases.

Chronic respiratory diseases are a significant health problem in the elderly and tend to relate to increasing age [1]. Aging and accumulating exposure to environmental toxins can lead to numerous anatomical, physiological, and immunological modifications of the respiratory system [2-8]. Previous studies investigated the aging respiratory system. A study of rats demonstrated collagen accumulation and progressive fibrosis of the aging lung [9]. Microscopic examination of aging human lungs shows increasing airspace size without evidence of destruction of the alveolar wall [10-12]. Plain radiographs reveal hyperinflation of the lungs and bullous spaces in the lungs of both normal and emphysematous patients [13]. Several computed tomography (CT) studies examining lung morphology in elderly revealed air trapping [6, 14, 15], a subpleural basal reticular pattern, lung cysts [16] and increases in the bronchoarterial ratio, which reflects bronchiectasis [16, 17].

Although CT studies of morphological changes in aging lungs are available, most are limited to a subgroup of urban dwellers. The results are not truly representative of the general Thai elderly population in respect of ethnicity, environment, and prevalent diseases.

The purpose of the present study was to describe morphological changes of lungs in elderly Thais without any respiratory illnesses in comparison with younger individuals.

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Materials and methods

Patient participants

The institutional review board of the Medical Faculty of Chulalongkorn University (Bangkok, Thailand) reviewed our study protocols and gave approval for additional limited CT examination and for submission of data for publication (IRB 296/56). Written informed consent to participate in this study and undergo the additional CT examination was obtained from each patient, or their nearest relative or legal guardian in the case of senile patients or those not capable of providing their own consent.

This cross-sectional study included prospectively selected patients was designed to evaluate the morphological changes in lungs by performing limited additional thoracic CT in Thai patients classified into three age groups; 20–40 years, 41–60 years, and >60 years.

The enrolled participants were Thai patients who had been referred for CT of the abdomen or head and neck at King Chulalongkorn Memorial Hospital from October 2013 to September 2014. Participants with symptoms or problems involving the respiratory system or related systems, which might affect morphological changes of the lungs defined by clinically constructed questionnaire were excluded from the study. Dyspnea was graded using the modified Medical Research Council breathlessness scales [18] (grade 0 = breathless with strenuous exercise, grade 1 = breathless when hurrying on level ground or walking up hill, grade 2 = breathless when walking on the level, grade 3 = breathless after walking about 100 yards, grade 4 = breathless at rest).

Exclusion criteria were active pulmonary diseases, any respiratory symptom other than grade 1 dyspnea, primary lung cancers or lung metastasis, morphological abnormalities on previous chest X-ray or CT images, any known chronic pulmonary disease, known cardiac failure with pulmonary edema or pulmonary hypertension at the time of the CT study, known connective tissue diseases affecting the respiratory tract, previous thoracic operations or radiation, previous trauma affecting lungs, and pregnancy. Any patients with confusion, inability to stay still in a supine position, or inability to hold their breath were also excluded from our study.

Sixty-seven consecutive asymptomatic patient volunteers (20 years or older) were enrolled after receiving complete comprehensible information concerning the purpose of this study. Smoking history in pack-years, dyspnea scores, and underlying disease were recorded. Seven participants failed to meet these criteria and were excluded from our study. The remaining 60 patient participants were 20 in each age group.

CT technique

Limited-sliced supine inspiratory and expiratory CT imaging of the thorax was performed using Somatoms sensation 16 (Siemens, Germany) and Discovery CT750 HD (GE healthcare, United Kingdom) with scanning parameters as follows; 0.75 mm collimation, slice thickness 1 mm, 100 kVp, 134 mA, and 0.625 mm collimation, slice thickness of 1 mm, 120 kVp, 165 mA, respectively. Images were acquired with 8 sequential axial slices; 4 slices on full inspiratory phase and other 4 slices on full expiratory phase to assess the degree of air trapping. The slices were performed at 4 levels: at the top of the aortic arch, at the carina, at the right inferior pulmonary vein, and at 2 cm above the right hemidiaphragm. Before scanning, participants were provided breathing instructions and practiced the breathing. No contrast medium was used in our protocol. However, patients may have received contrast medium for their primary study after the additional study CT chest was completed. CT scans were reconstructed using an algorithm with high spatial resolution.

Assessment of CT features

Standard lung window settings were routinely used for the evaluation (level –500 Hounsfield units (HU), width 1500). All images were rendered anonymously and researchers were blinded to the clinical data. Two researchers; including a thoracic radiologist (NP with 15 years' experience of thoracic CT) and a resident training in diagnostic radiology (NL with 3 years' experience of radiology), independently reviewed all sections. Where the two readers could not reach a consensus, they scored the sections together. The final consensus results were recorded. CT features recorded included the presence, extent, grading, and distribution of air trapping, bronchiectasis, bronchial wall thickening, and reticulation. Other significant features were recorded as remarks.

The degree and lobar involvement of air trapping were defined from consensus of visual assessment and measurement of the mean lung attenuation. In normal lungs, the mean increase in lung attenuation at expiration should be approximately at 110 HU [15].

Measurement of mean lung attenuation was performed by freehand drawing regions of interest (ROIs) at a work station (Fuji PACS, Japan) in selected areas, which were the areas of most correspondence between inspiration and expiration. The mean lung attenuation value during inspiration was subtracted from that during expiration at each level. If visual assessment was consistent with air trapping and mean lung attenuation was increasing less than 110 HU, then the area was recorded as air trapping. The ROIs excluded the chest wall and large hilar vessels. Grading of air trapping was defined as: lobular, composed of small areas of hypoattenuation that corresponded to 1 or 2 adjacent secondary pulmonary lobules in 1 or 2 regions per lung level, 3 or more areas of lobular air trapping observed alternating with areas of normally attenuating lung, usually in a multilobular distribution, extensive with contiguous areas of air trapping in more than 3 adjacent pulmonary lobules, and sub-segmentally or lobar in distribution.

Reticulation within basal segments or other segments of lung was recorded. A reticular pattern adjacent to thoracic vertebral osteophytes was not included. Bronchiectasis was recorded and defined as bronchial dilatation with internal diameter of bronchus greater than the adjacent pulmonary artery [17], lack of tapering of bronchi, and identification of bronchi within 1 cm of the pleural surface [19]. Degree of bronchiectasis was defined as cylindrical, varicosities or cystic. Lobar involvement was also noted.

For the last important CT feature collected during this study, the presence or absence of bronchial wall thickening with involvement of lobes was then determined by visual analysis. For ambiguous cases, measurements were performed using a work station (Fuji PACS, Japan) at 5× magnification and measurement using electronic calipers, with wall thickness derived from these measurements (T = (D–L)/2) (**Figure 1**) [20]. Normally, the mean T/D ratio (bronchial wall thickness/ total diameter of bronchus) is approximately 0.2 [17]. Bronchial wall thickening was recorded when the T/D ratio was more than 0.2.

Statistical analysis

Statistical analyses were conducted using IBM SPSS Statistics for Windows, version 20 (IBM corporation, Armonk, NY, USA) and program R version 3.1.1 (GNU General Public License, USA). The three groups were compared using a Pearson chi-square test. A ROC curve was used to determine new age groups according to zero count in some of the characteristics of the original age groups. The comparison of variables of the new age groups were compared using a Fisher exact test and binomial proportion test.

Results

Demographic data are shown in **Table 1**. Patients were equally stratified to three age groups, group 1, 2, and 3 with a mean age of 30.5, 50.4, and 66.7 years old, respectively.

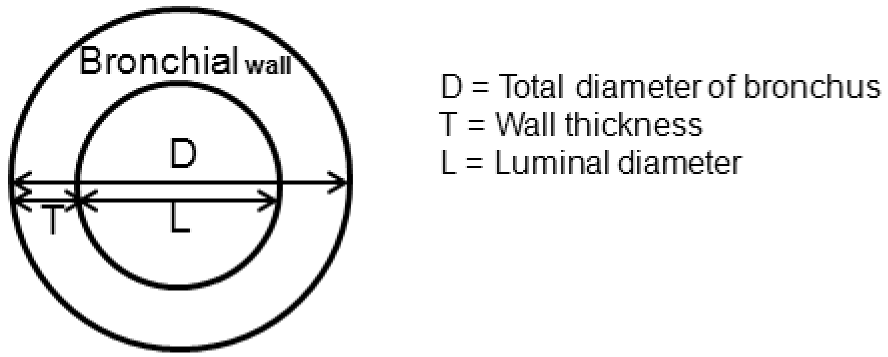


Figure 1. Bronchial wall thickening

Table 1. Demographic data

	Group 1	Group 2	Group 3	P^b
Range (age)	20–40	41–60	≥61	
Median	32	51	64.5	
Mean (Standard deviation)	30.5 (6.1)	50.4 (4.9)	66.7 (5.7)	
Number of participants	20	20	20	
Male (%)	17 (85)	17 (85)	8 (40)	0.01
P-value of the proportional test (H_0: male: female = 0.5)	<0.05	<0.05	0.50	
Smoking	4	10	5	0.09
Smoking history (Pack-years)[a]	0 (0–2.5)	0.05 (0-40)	0 (0-60)	

[a]Data are medians, with ranges in parentheses, [b]Pearson chi-square test

Pearson chi-square statistics revealed an association between age group and sex ($P = 0.01$). The proportion test demonstrated the unequal distribution of sex among age groups ($P < 0.05$ in the age group 1 and 2). Sixteen of the subjects in the youngest age group had never smoked, while 10 and 15 participants in the middle and oldest age groups had no smoking history, respectively. A Pearson chi-square test showed no relationship between age group and smoking status. A Pearson chi-square statistic showed a relationship between age group and the presence of air trapping, bronchiectasis, and bronchial wall thickening in CT images as seen in **Table 2** ($P < 0.01$, $P = 0.03$, and $P = 0.03$, respectively). The results showed that air trapping was strongly correlated with age. However, it is difficult to conclude such correlation with bronchiectasis and bronchial wall thickening because there were groups that had zero count, which increases the rate of errors from the chi-square test. Reticulation was found in only one patient in the middle age group (**Figure 2**). There was no significant difference between the age groups ($P = 0.36$).

Because there were no bronchiectasis or bronchial wall thickening found in the youngest age group, a ROC curve was used to re-categorize participants into two age categories (<56 and >56 years old) to reduce the error from the Pearson chi-square test. Sensitivity and specificity of the coordinate of the ROC curve for bronchiectasis (**Figure 3 left**) at the age of 56 years were 70% and 68%, respectively (**Table 3**). The sensitivity and specificity of the co-ordinate of the ROC curve for bronchial wall thickening (**Figure 3 right**) at age 56 years was 78% and 69%, respectively (**Table 3**).

Fisher's exact test was used to determine the differences in bronchiectasis and bronchial wall thickening between the two groups (at ≤56 years and age >56 years) because the count in first group was less than 5 (**Table 4**) . Fisher's exact test revealed a relationship between age and presence of bronchiectasis and bronchial wall thickening in CT images ($P = 0.04$ and $P = 0.02$, respectively). Therefore, the bronchiectasis and bronchial wall thickening were related to age.

Table 2. Correlation between each outcome and age group

CT scan outcome	Age group 1	Age group 2	Age group 3	*P**
Air trapping present	5	7	18	<0.01
Air trapping absent	15	13	2	
Reticulation present	0	1	0	0.36
Reticulation absent	20	19	20	
Bronchiectasis present	0	4	6	0.03
Bronchiectasis absent	20	16	14	
Bronchial wall thickening present	0	3	6	0.03
Bronchial wall thickening absent	20	17	14	

*Pearson chi-square test

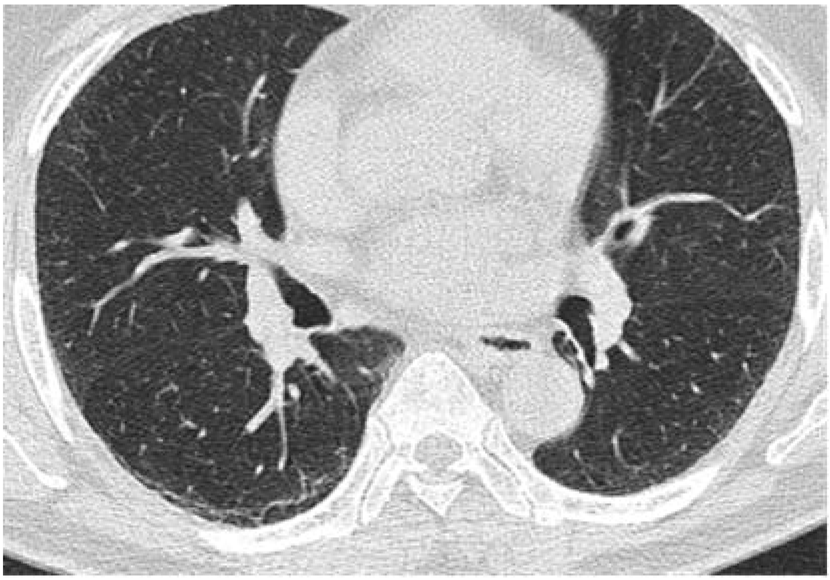
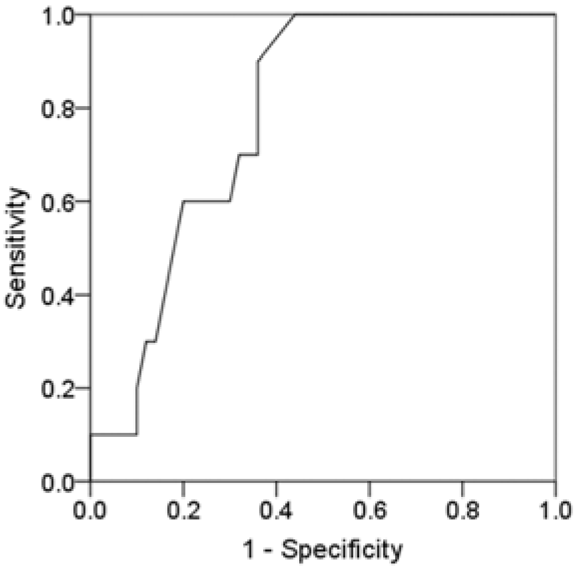


Figure 2. Basal reticulation appears in RLL in one participant in the middle age group.



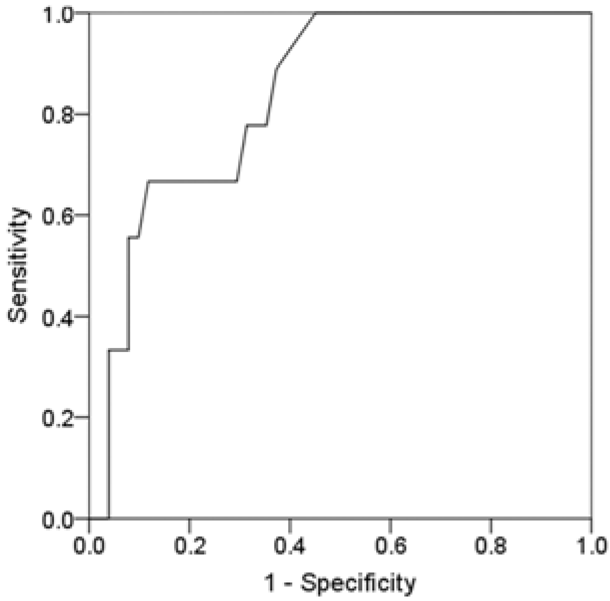


Figure 3. The ROC curves for age with bronchiectasis (left) and age with bronchial wall thickening (right)

Table 3. Sensitivity and specificity of the coordinate of the ROC curve at age 56

	Bronchiectasis	Bronchial wall thickening
Sensitivity	70%	78%
Specificity	68%	69%

Table 4. Correlation between each outcome and age group

Parameters	Age ≤56	Age >56	*P*
Number	37	23	0.09
Bronchiectasis	3	7	0.04
Bronchial wall thickening	2	7	0.02

A Pearson chi-square statistic showed no relationship between smoking status and the presence of air trapping, reticulation, bronchiectasis and bronchial wall thickening in CT images of any participant (P >0.10) (**Table 5**).Air trapping was found in patients in every age group (**Table 6**). However, in the youngest age group, it was only in both lower lobes, and in all age groups, air trapping was mostly found in both lower lobes (P <0.01) (**Table 7**). Like air trapping, bronchiectasis and bronchial wall thickening were also mostly seen in both lower lobes; however, there is not sufficient evidence to conclude that there is an association between age and lobes (P = P 0.21 in bronchiectasis and P = 0.09 in bronchial wall thickening) (**Tables 8, 9, and 10**).

Table 10 show degree of air trapping, which was equally distributed into lobular and geographic types. Extensive air trapping was found less often. There was an association between age and extensive air trapping (P = 0.02). In case of bronchiectasis, there was only cylindrical bronchiectasis (**Table 11**).

Table 5. Correlation between each outcome and smoking status in all participants

CT imaging outcome	Smoking	No smoking	*P*
Air trapping present	10	20	>0.10
Air trapping absent	9	21	
Reticulation present	1	0	>0.10
Reticulation absent	18	41	
Bronchiectasis present	3	7	>0.10
Bronchiectasis absent	16	34	
Bronchial wall thickening present	3	6	>0.10
Bronchial wall thickening absent	16	35	

[a]Binomial proportion test, [b]Fisher’s exact test

Table 6. Distribution of air trapping, bronchiectasis and bronchial wall thickening in each group

Parameter	Lobe	Age group 1	Age group 2	Age group 3	Total number in each lobe (%)
Number of air trapping	RUL	0	1	5	6 (8)
	RML	0	1	1	2 (3)
	RLL	5	6	17	28 (39)
	LUL	0	1	5	6 (8)
	Lingular	0	1	1	2 (3)
	LLL	4	7	17	28 (39)
Bronchiectasis	RUL	0	1	2	3 (13)
	RML	0	4	1	5 (22)
	RLL	0	2	3	5 (22)
	LUL	0	1	0	1 (4)
	Lingular	0	1	0	1 (4)
	LLL	0	2	4	6 (26)
Bronchial wall thickening	RUL	0	2	2	4 (15)
	RML	0	2	2	4 (15)
	RLL	0	2	5	7 (26)
	LUL	0	2	2	4 (15)
	Lingular	0	0	0	0 (0)
	LLL	0	2	6	8 (30)

RUL = right upper lobe, RML = right middle lobe, RLL = right lower lobe, Lingular = lingular segment of LUL, LUL = the rest of left upper lobe, LLL = left lower lobe

Table 7. Comparison of air trapping in lower lobes and other lobes in all participants

Air trapping	Other lobes	LLL+RLL	*P*[a]
Positive	16	56	<0.01
Negative	224	64	

[a]Pearson chi-square test, LLL = left lower lobe, RLL = right lower lobe,

Table 8. Distribution of bronchiectasis in total participants

	RUL	RML	RLL	LUL	Lingular	LLL
Positive	3	5	5	1	1	6
Negative	57	55	55	59	59	54

P = 0.21 by Pearson chi-square; RUL = right upper lobe, RML = right middle lobe, RLL = right lower lobe, Lingular = lingular segment of LUL, LUL = the rest of left upper lobe, LLL = left lower lobe

Table 9. Distribution of bronchial wall thickening in total participants

	RUL	RML	RLL	LUL	Lingular	LLL
Positive	4	4	7	4	0	8
Negative	56	56	53	56	60	52

P = 0.09 by Pearson chi-square; RUL = right upper lobe, RML = right middle lobe, RLL = right lower lobe, Lingular = lingular segment of LUL, LUL = the rest of left upper lobe, LLL = left lower lobe

Table 10. Degree of air trapping in each age group

Air trapping	Age group 1	Age group 2	Age group 3	Total	*P*[a]
Lobular	3	4	5	12	0.11
Geographic	2	2	8	12	0.09
Extensive	0	1	5	6	0.02

[a]Pearson chi-square test

Table 11. Degree of bronchiectasis in each age group

Degree	Age group 1	Age group 2	Age group 3	Total
Cylindrical	0	4	6	10
Varicose	0	0	0	0
Cystic	0	0	0	0

Figure 4. Demonstrates geographic degree of air trapping in both lower lobes of participant from elderly group

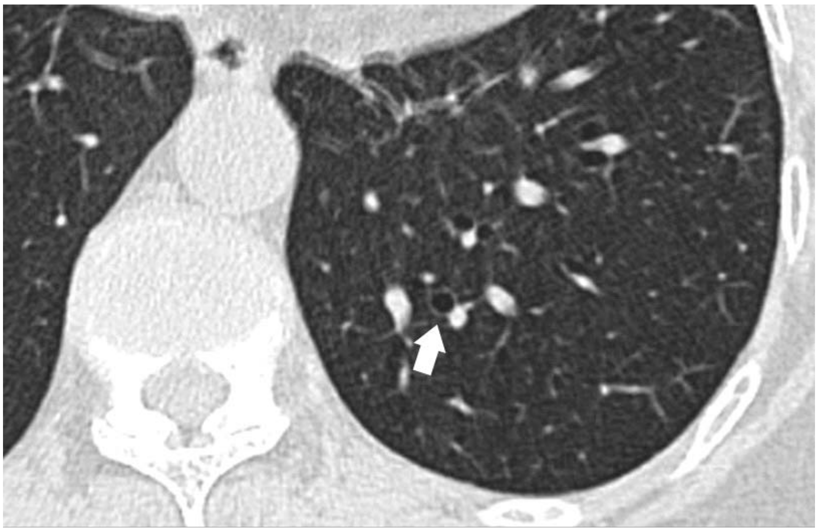


Figure 5. Signet ring sign indicates bronchiectasis in LLL in one participant (arrow).

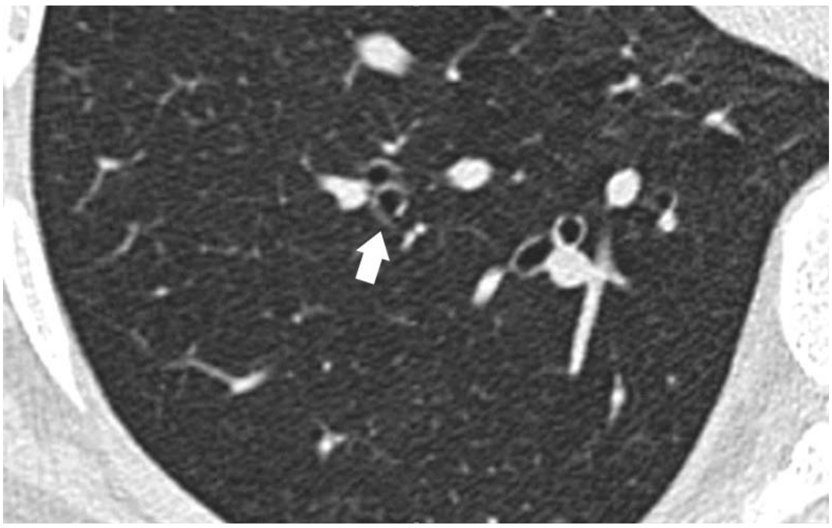


Figure 6. Bronchial wall thickening seen in RLL in elderly participant (arrow).

Discussion

We found that asymptomatic elderly participants had high frequency of air trapping, bronchiectasis, and bronchial wall thickening, which were independent of smoking history. These features are clinically important because of their potential as lung disease markers. Using these parameters in a clinical setting may prevent unnecessary investigation and follow up. So the results may reduce the potential confusion with disease, which results in unnecessary follow up investigations or treatment, or both, with potential expense and possible complications.

Air trapping is a term to describe retention of gas in all or part of a lung in the expiratory phase [4]. In one CT study, it was defined as an approximately 111.9 ± 46.3 (mean ± standard deviation) HU increase in mean lung attenuation in all three levels [5]. We showed a higher prevalence of air trapping in the older patients than younger patients (P <0.01). This finding is consistent with previous reports [6]. Lee et al. found that air trapping significantly increased with age and that there was a higher frequency of air trapping in smoking patients despite lacking of statistical significance [6]. Consistent with our findings Tanaka et al. showed no significant difference in air trapping between nonsmokers and smokers (P > 0.1 in our study) [15]. There was more frequent air trapping in lower lungs (P <0.01). This finding corresponds with that of Tanaka et al. [15]. Air trapping in our study was of the lobular and geographic types. Extensive air trapping was found less frequently, but it associated with increasing age (P = 0.02). However, because there were low counts in some categories, the study may have lacked the power to be conclusive.

We were not able to evaluate the cause of the air trapping in the present study because the relationship with histopathological findings could not be examined. However, there hypotheses for the cause of air trapping in lungs of elderly people. Progressive decline in respiratory and cardiac function causes alteration of alveolar dead space and shunts, possibly contributing to air trapping [4].

We found significant relationship between bronchiectasis and age (P =0.035). The result was consistent with the study reported by Matsuoka et al. They reported that the bronchoarterial ratio was correlated with age and that there was significant difference between younger individuals and individuals older than 65 years (r = 0.77, P < 0.01) [17]. Most bronchiectasis was found in both lower lobes; however, no significant difference was observed (P = 0.21). Bronchiectasis was not influenced by smoking status (P > 0.10).

Bronchial wall thickening can be defined as a T/D ratio more than 0.2 [17]. In our study, the prevalence of bronchial wall thickening was more frequently present in older patients than younger patients (P = 0.02). Smoking status was not a predictor of bronchial wall thickening (P > 0.1). However, in the study by Matsuoka et al., no significant correlation was seen between the T/D ratio and age. Moreover, no significant differences in bronchoarterial ratio and T/D ratio were observed between smokers and nonsmokers, but in the elderly group, the T/D ratio was significantly higher in smokers than in nonsmokers (P = 0.02) [17]. The discrepancy could be the result of the small number of participants in both studies and suggests the need for validation.

Reticulation showed no significant difference between the age groups in our study (P = 0.36). However, in a previous study by Copley et al., there was a statistical difference in reticulation between individuals aged over 75 years when compared with those younger than 55 years. However, this may be the result of the lower mean age of our older age group compared with the previous study (66.7 ± 5.7 and 80.6 ± 4.2 years old, respectively) [16].

The strength s of our study were that we evaluated and correlated several CT features in one study. Furthermore, we performed a subgroup analysis of the basis of smoking status, and extent of CT features as described.

There are several limitations to our study. First, the sample size of this study was small. This could increase the rate of type 2 error (false negative). To improve this study, more participants should be included by either extending the length of the study or initiating a multicenter trial. Next, the group did not consist only of nonsmoker, but also of active smokers and ex-smokers. Nevertheless, as described we found that smoking status was not a predictor of outcome; so our study might be representative of the general Thai population. Another limitation was an unequal proportion of male and female patients, which was significantly different in the age groups 1 and 2 (P < 0.05). A proportion test demonstrated that only the oldest age group contained an equal number of men and women. If sex was a confounder and had an effect on the CT findings, results could be biased toward the finding for the Thai male population.

Unfortunately, we did not perform pulmonary function tests. However, in the past study, there was no correlation between pulmonary function and CT features [14], so we could define asymptomatic participants based on clinical data from our structured questionnaire.

Because participants were prospectively recruited and consisted in part of young patients, our protocol was designed to minimize radiation dose. This limited us to using only 8 sequential slices with fixed 100–120 kVp protocol. The use of noncontiguous slices limited evaluation. We did not fully investigate extension of bronchiectasis. However, our results were nevertheless significant. Nor did our protocol allow acquisition of additional prone scans, limiting identification of atelectasis and a subpleural line was possible. Actually, reticulation was found in only one patient, so a prone scan might have been redundant.

There was unavoidable selection bias because we only recruited patient participants without respiratory symptoms; therefore, it might not truly be representative of the entire Thai population.

Conclusion

Asymptomatic older patient participants had greater prevalence of air trapping, bronchiectasis, and bronchial wall thickening than the younger patient participants in our study population. All of the described CT features were independent of smoking history. Air trapping was most common in both lower lobes. Extensive degree of air trapping also correlated with aging.

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Conflict of interest statement

The authors have no conflicts of interest to declare.

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