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Detection of secondary causes of spontaneous pneumothorax: comparison between computed tomography and chest X-ray

Short Title:

Thoracic CT for the detection of causes of spontaneous pneumothorax

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Conflict of interest: none declared.

Abstract

Purpose: The aim of this study was to compare the effectiveness of chest X-rays to that of thoracic computed tomography (CT) for the detection of the causes of secondary spontaneous pneumothorax (SP).

Methods: A prospective cohort of patients diagnosed with SP was studied. All chest X-rays and CT examinations of the patients were reviewed retrospectively by an expert radiologist blinded to clinical data. The concordance between the CT examination and chest X-ray was assessed using the Cohen Kappa coefficient (κ), based on a bootstrap resampling method.

Results: A total of 105 patients with SP were included. There were 78 men and 27 women, with a mean age of 34.5 years $\pm$ 14.2 (SD) (range: 16-87 years). Of these, 44/105 (41%) patients had a primary SP and 61/105 (59%) had a secondary SP due to emphysema (47/61; 77%), tuberculosis (3/61, 5%), lymphangioliomyomatosis (3/61; 5%), lung cancer (2/61, 3%) or other causes (6/61; 10%). Apart from pneumothorax, CT showed abnormal findings in 85/105 (81%) patients and chest X-rays in 29/105 (28%). Clinically relevant abnormalities were detected on 62/105 (59%) CT examinations. The concordance between chest-X ray and CT was fair for detecting emphysema ($\kappa = 0.39$; 95% CI: 0.2420 - 0.55), moderate for a mass or nodule ($\kappa = 0.60$; 95% CI: 0.28 - 0.90), fair for alveolar opacities ($\kappa = 0.39$; 95% CI : -0.02 - 1.00), and slight for interstitial syndrome ($\kappa = 0.20$; 95% CI : -0.02 - 0.85).

Conclusion: Chest X-ray is not sufficient for detecting the cause of secondary SP. As the detection of the cause of secondary SP may alter the therapeutic approach of SP and long-term follow-up, the usefulness of a systematic CT examination should be assessed in a prospective trial.

Keywords: Spontaneous pneumothorax; Secondary pneumothorax; Computed tomography (CT), Emphysema; Chest X-ray

Introduction

The American College of Chest Physicians [1], British Thoracic Society [2] and European Respiratory Society [3] guidelines do not recommend the routine use of computed tomography (CT) for patients with a first episode of spontaneous pneumothorax (SP). Following these guidelines, CT is recommended only for uncertain or complex situations.

Primary spontaneous pneumothorax (PSP) is defined as a pneumothorax that occurs in patients without a clinically apparent lung disease, whereas a secondary spontaneous pneumothorax (SSP) is a complication of a pre-existing lung disease [4]. PSP is common in young adults, with an incidence of 7.4 to 18 per 100,000 males and 1.2 to 6 per 100,000 women [4]. The etiologies of PSPs are not well known. The risk increases with body size [4] and tobacco smoking, with a relative risk of 20 reached in a dose-dependent manner [4].

Although PSPs arise in patients without any clinically apparent lung disease, these patients frequently exhibit emphysema-like changes on chest CT [5]. Studies have investigated the presence of emphysema-like changes on CT and their correlation with pneumothorax recurrence, with contradictory results [6]. According to some authors, this is a strong argument for not employing CT in the management of these patients [6].

However, the identification of the cause of a SSP is crucial, because immediate and long-term management of SSP differs from that of a PSP, along with significantly more severe consequences. Guidelines suggest that all patients with a SSP should be admitted to hospital [1,2]. The recurrence rate of a SSP is likely to be higher than that of a PSP [4]. Moreover, the outcome of surgical treatment for secondary spontaneous pneumothorax (recurrence of pneumothorax, hospital mortality, postoperative complications) depends on underlying diseases [7,8].

The main etiology of SSP is chronic obstructive pulmonary disease [4]. We have previously reported a high prevalence of emphysema in tobacco and cannabis smokers hospitalized for SP [9]. Further etiologies of SSPs are other airway diseases, infectious lung disease, interstitial lung disease, or connective-tissue disease associated with lung disease, and cancer [4]. There is a gap between the guidelines that do not recommend the routine use of CT for patients with SPs, and the treatment and the follow-up who depend on the underlying diseases, so questioning the use of chest X-ray that may be not sensitive enough to identify an underlying disease.

The aim of this study was to compare the effectiveness of chest X-rays to that of thoracic CT in the detection of secondary causes of SP.

Material and Methods

Ethical considerations

The study protocol was approved by the Institutional Review Board of the French Society of Thoracic and Cardiovascular Surgery (CERC-SFCTCV-2016-8-8-22-26-27-GoVa) with a waiver for informed consent.

Patients

The data of all patients admitted to the “SOS pneumothorax” unit of Tenon University Hospital were prospectively recorded from January 1, 2012 to May 1, 2013. “SOS pneumothorax” is a tertiary referral unit dedicated to the management of patients with pneumothorax consisting of a referent pulmonologist and thoracic surgeons open 24H/24. All patients presented with pneumothorax on chest X-ray. During the first period from January 2012 to January 2013 (Period 1), thoracic CT examinations were performed for patients older than 40 years presenting with active tobacco abuse of more than 15 pack-years, or for those with an abnormal chest X-ray (apart from pneumothorax). Chest X-ray was considered as showing abnormal findings by the pulmonologist or the thoracic surgeons. Given that clinicians observed a high incidence of lung lesions in patients with SP, sometimes less than 40 years or non smoker, patients with SP underwent thoracic CT systematically from February to May 2013 (Period 2). Patients from the database were reviewed and only those with a SP who had undergone CT examination were included retrospectively in the study, whereas patients with an iatrogenic or traumatic pneumothorax and patients who did not undergo CT examination were excluded.

Between January 2012 and May 2013, 171 patients with SPs were included in this study. Forty-four patients were excluded from the analysis: 11 had an iatrogenic pneumothorax and 23 had a traumatic pneumothorax. Figure 1 shows patients inclusion and exclusion into the study

Clinical assessment

For each patient, the following characteristics were analyzed: age, gender, weight, size, body mass index (BMI), etiology of the pneumothorax, personal and family histories of a pneumothorax and type of pneumothorax, as well as pneumothorax treatment. Tobacco and

cannabis consumptions were assessed on arrival at the hospital and were respectively quantified in pack-years (PYs) and joint-years (JYs). Each file was discussed in a multidisciplinary manner by radiologists and clinicians in an effort to determine whether it was a primary or secondary pneumothorax. The diagnosis is based on a body of clinical, radiological and histological arguments, when available.

Imaging evaluation

Chest X-rays examinations were obtained in posterior-anterior projection using a digital radiography system (Digital Diagnost, Philips Healthcare) with a focal spot size of 1.25mm, distance from source to detector of 180cm, 120kVp, and 200-250mA. Chest X-rays were performed at the time of diagnosis. All chest X-rays were retrospectively reviewed by a radiologist (AK, with more than 20 years' experience in thoracic imaging), who was blinded to the clinical data. Parenchymal abnormalities were assessed according to the Fleischner Society definition [10]. For each X-ray, the abnormalities were analyzed as follows: emphysema, nodule or mass, alveolar opacity, and interstitial syndrome.

CT examinations were obtained using a plain CT acquisition of the whole thorax with 64-section CT units Brilliance® 64 (Philips Healthcare) or HD 750® (General Electric Healthcare) with the following parameters: peak tube potential, 120kV; auto MA exposure with 1-mm collimation and beam pitch 1; reconstruction slice thickness, 1 mm. Images were obtained with a standard and high frequency algorithm. CT examinations were performed either at the time of diagnosis or during follow-up.

Image analysis

All thoracic CT and chest X-ray examinations were retrospectively reviewed by the same radiologist, but independently. Thoracic CT examinations were reviewed for morphological parenchymal abnormalities using both standard and high-frequency algorithms with standard multiplanar reformatting, maximum intensity projection, and minimum intensity projection applied to the volume. Parenchymal abnormalities were assessed according to the Fleischner Society definition [10]. For each CT examination, the abnormalities analyzed were as follows: emphysema, nodule or masse, alveolar opacity, and interstitial syndrome. Bullae were considered as a clinically-relevant lesion if more than five bullae or bullae larger than 1 cm were present. A nodule was considered as clinically-relevant

when the lesion was ≥ 4 mm. Ground glass image resulting from pulmonary reexpansion was not considered as a clinically-relevant lesion.

Statistical analyses

The data were analyzed using SPSS (Statistical Package for the Social Sciences). Quantitative variables were expressed as means $\pm$ standard deviations (SD) and ranges. Qualitative variables were expressed as raw numbers, proportions and percentages. Comparisons between the groups were performed using the Student *t*, Mann-Whitney or McNemar test for quantitative variables and Chi-squared (χ^2) or Fisher test for qualitative variables. A *P* value < 0.05 was considered statistically significant. Univariate analysis by logistic regression was used to identify a subgroup of patients who should benefit from a thoracic CT examination. Unadjusted odds ratio (OR) with 95% confidence interval (CI) were reported. Multivariate analysis was performed using logistic regression. The variables associated with a benefit from a thoracic CT examination (*P* < 0.10) in the univariate analysis were included in multivariate model.

For each of imaging abnormalities, the concordance between the CT and chest X-rays was assessed using the Cohen Kappa coefficient (κ) with a 95% confidence interval, based on a bootstrap resampling method.

Results

Study population

The study population consisted of 105 patients who had undergone CT examination. There were 68 men and 37 women with a mean age of 34.5 ± 14.2 (SD) years (range: 16-87 years); of these, 44/105 (41%) patients exhibited a PSP and 61/105 (59%) a SSP (Table 1). Overall, 90/105 (86%) patients were tobacco smokers and 40/105 (39%) cannabis smokers; 42/105 (40%) patients had a personal history of SP and 6/105 (5.7%) a familial history of SP. Surgery was performed in 57/105 (54%) patients.

X-ray and CT abnormalities

Chest X-rays showed abnormal findings apart from pneumothorax in 29/105 (27.6%) patients with a total of 32 detected abnormalities (Table 2), consisting in 23/32 (72%) emphysema or

apical bullae, 5/32 (16%) masses or nodules, 2/32 (6%) interstitial syndromes and 2/32 (6%) alveolar opacities.

Among the 105 CT examinations, apart from pneumothorax, 85/105 (81%) showed abnormal findings with a total of 102 detected abnormalities (Table 2). Emphysema or apical bullae were 76/102 (74.6%) abnormalities, masses or nodules were 14/102 (13.7%) abnormalities, interstitial syndromes were 8/102 (7.8%) abnormalities and alveolar opacities were 4/102 (3.9%) abnormalities.

Among the 76 CT examinations on which emphysema or apical bullae were present, 50/76 (66%) showed clinically-relevant lesions (emphysema or more than five bullae or bullae larger than 1 cm). The remaining 26/76 (34%) CT examinations showed non-clinically relevant bullae (less than five bullae and less than 1cm). Of the 14 CT examinations that showed a mass or nodule, 3/14 (21%) nodules were < 4 mm, thus not clinically relevant. Among the 4 alveolar opacities present on CT in 4 patients, 1/4 (25%) was not clinically relevant, resulting from passive atelectasis. Among the 8 interstitial syndromes present on CT in 8 patients, 1/8 (13%) was not clinically relevant exhibiting a ground glass image resulting from pulmonary reexpansion. Lastly, 62/105 (59%) CT revealed clinically relevant abnormalities.

Concordance between chest-X ray and CT-scan

Among the 105 patients, 62/105 (59%) patients had abnormal CT findings with clinically relevant abnormalities and 29/105 (27.6%) had chest X-rays that showed abnormal findings (Tables 2 and 3). In 35/105 (33%) patients, CT examinations showed abnormal findings and chest X-rays without any specific abnormality. The concordance between chest CT examination and chest X-ray was fair for emphysema ($\kappa = 0.39$; 95%CI: 0.24 - 0.55), moderate for the detection of a mass or nodule ($\kappa = 0.60$; 95%CI: 0.28 - 0.90), fair for alveolar opacities ($\kappa = 0.39$; 95%CI: -0.02 - 1.00) and slight for interstitial syndrome ($\kappa = 0.20$; 95%CI: -0.02 - 0.85) (Figure 2).

Regarding the diagnosis of emphysema (n=50 patients), all patients with abnormal findings on chest X-rays except 2, 21/50 (42%) were associated with abnormal findings on CT (Table 3). On the opposite among the 50 patients with emphysema on CT, 29/50 (58%) had no visible emphysema on chest X-rays (Figure 3). Regarding the diagnosis of lung mass or nodule (n=11 patients), all patients with masses and nodules seen on chest X-rays (5/11;

46%) were associated with masse or nodule on CT. On the opposite among the 11 patients with mass or nodules on CT, 6/11 (54%) had no visible masse or nodule on chest X-rays. Regarding the diagnosis of alveolar opacities (n=3 patients), 2 patients with alveolar opacities were detected on CT, but not seen on chest X-rays. Finally, regarding the diagnosis of interstitial syndrome (n=7 patients), 6 patients had interstitial syndromes visible on CT, but not seen on chest X-rays (Figure 4). At multivariate analysis, only older age was associated with CT abnormalities.

Secondary spontaneous pneumothorax

The first cause of SSP was emphysema (47/61; 77%), followed by tuberculosis (3/61, 5%), lymphangioleiomyomatosis (3/61; 5%), lung cancer (n=2/61; 3%), and other causes (6/61; 10%) (Table 2). Patients with SSP were older (44 ± 16.7 [SD] years; range: 18-87 years) than those with PSP (31 ± 8.2 [SD] years; range: 16-51 years) ($P < 0.005$). The hospital stay length was greater in the SSP group, (13.2 ± 9.3 [SD] days; range: 2-22 days) than in the PSP group (7.9 ± 9.3 [SD] days; range: 2-23 days) ($P < 0.001$) (Table 4). At multivariate analysis, only age ($P < 0.0001$) and family SP history ($P = 0.0382$) were associated with a SSP.

Discussion

The objective of our study was to compare the effectiveness of chest X-rays to that of thoracic CT for the detection of secondary causes of SPs. In this study, chest X-ray examination has limitation for detecting secondary causes of SPs with only 27% (29/105) abnormal findings. Among the patients with normal findings on chest X-rays, thoracic CT examination detected clinically significant lesions in 33% (35/105) patients consisting mainly of emphysema, masses, or nodules, but also interstitial syndrome and alveolar opacities. Other authors have already suggested that chest X-rays examination result in underdiagnosed SSP [11,12].

The concordance between chest X-rays and thoracic CT was moderate for the detection of masses or nodules, mediocre for the detection of emphysema and alveolar opacities, and poor for the detection of interstitial syndrome. Similar results were observed by Padley et al. in the diagnosis of chronic diffuse infiltrative lung disease in 86 patients [13]. Of the patients with normal findings on chest X-rays, 42% exhibited diffuse infiltrative lung disease on CT. More recently, several studies showed that CT is more sensitive than chest X-

ray in the early detection of community-acquired pneumonia [14] or pneumonia in immunocompromised patients with neutropenic fever [15].

Early detection of SSPs is paramount to adapt therapeutic management, implement appropriate follow-up, or optimize the management of underlying diseases. For lymphangioleiomyomatosis, the American Thoracic Society [16] recommends ipsilateral pleurodesis after the initial pneumothorax. In addition, everolimus has been shown to be effective in preliminary studies [17]. An early diagnosis associated with an early treatment is likely to slow down the disease evolution. Furthermore, Maskell and Rahman reported that “imaging techniques have improved, it is becoming apparent that even these presumed healthy patients might have underlying lung abnormalities, and the traditional description of primary and secondary pneumothorax could be too simplistic.” [18]. A better etiological understanding and the identification of at-risk groups are likely to facilitate a more personalized approach.

Routine thoracic CT examination is likely to induce additional costs and irradiation, which may be problematic in young people. Low-dose or ultra-low-dose thoracic CT could be an option to decrease radiation dose. An ultra-low-dose thoracic CT could be an alternative to chest X-ray, providing more data at a similar radiation dose [19].

Our study has some limitations. First, it is a monocentric and retrospective study of patients who did undergo thoracic CT examination. In addition, as a tertiary care pneumothorax center, the recruitment bias must be noted with more SPS and more comorbidities than a primary health care center. So, our results cannot be extrapolated to a more general population of patients with pneumothorax.

In conclusion, chest X-ray proves to be insufficient for detecting a SSP. The possibility of an SSP should be considered in every patient with SP. Current guidelines for diagnosing SPs result in underdiagnosis of SSP. Given that detecting an SSP might change pneumothorax treatment and any long-term follow-up, the use of a systematic CT examination should now be assessed in this indication in a prospective trial.

Conflicts of interest

The authors have no conflicts of interest to disclose in relation with this article.

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Figure captions

Figure 1. Flow chart diagram of patient inclusion and exclusion.

Figure 2. Graph shows concordance between chest X-ray and CT examination (κ coefficient with 95% standard deviation for each abnormality).

Figure 3. 66-year-old man with pulmonary emphysema. A, Chest X-ray in anterior posterior projection shows no significant abnormality. B, CT image in the axial plane shows centrilobular emphysema (arrow), paraseptal emphysema (white arrowhead) and subcutaneous emphysema (black arrowhead).

Figure 4. 31-year-old woman with lymphangioleiomyomatosis. A, Chest X-ray in anterior posterior projection shows no significant abnormality. B, Thoracic CT image in the axial plane shows thin walled cysts of variable sizes (arrows) surrounded by normal lung parenchyma.

Table 1. Characteristics of patients with spontaneous pneumothorax.

Table 2. Chest X-ray and CT show abnormalities.

Table 3. Comparison between chest X-ray and thoracic computed tomography for the detection of clinically-relevant lesions in 105 patients with spontaneous pneumothorax.

Table 4. Etiologies of secondary spontaneous pneumothorax.

205 patients admitted for pneumothorax confirmed by chest X-ray

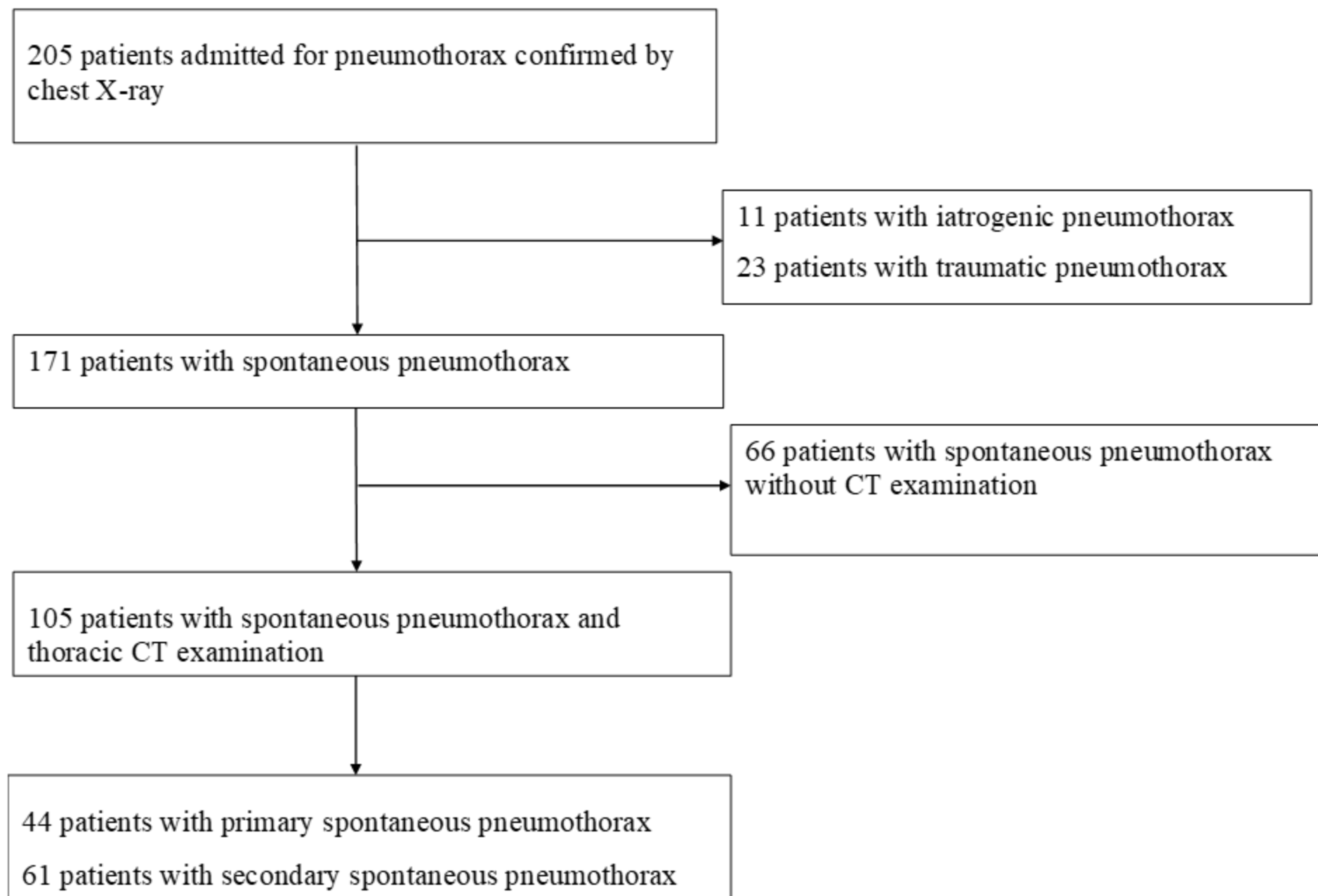
11 patients with iatrogenic pneumothorax
23 patients with traumatic pneumothorax

171 patients with spontaneous pneumothorax

66 patients with spontaneous pneumothorax without CT examination

105 patients with spontaneous pneumothorax and thoracic CT examination

44 patients with primary spontaneous pneumothorax
61 patients with secondary spontaneous pneumothorax

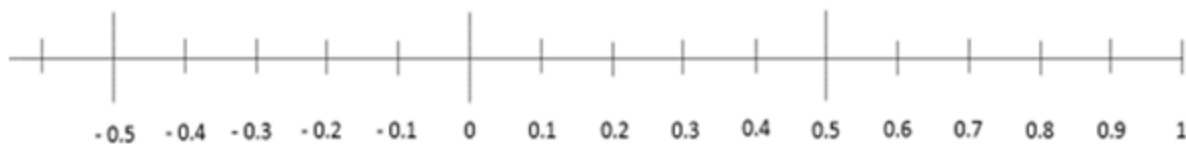


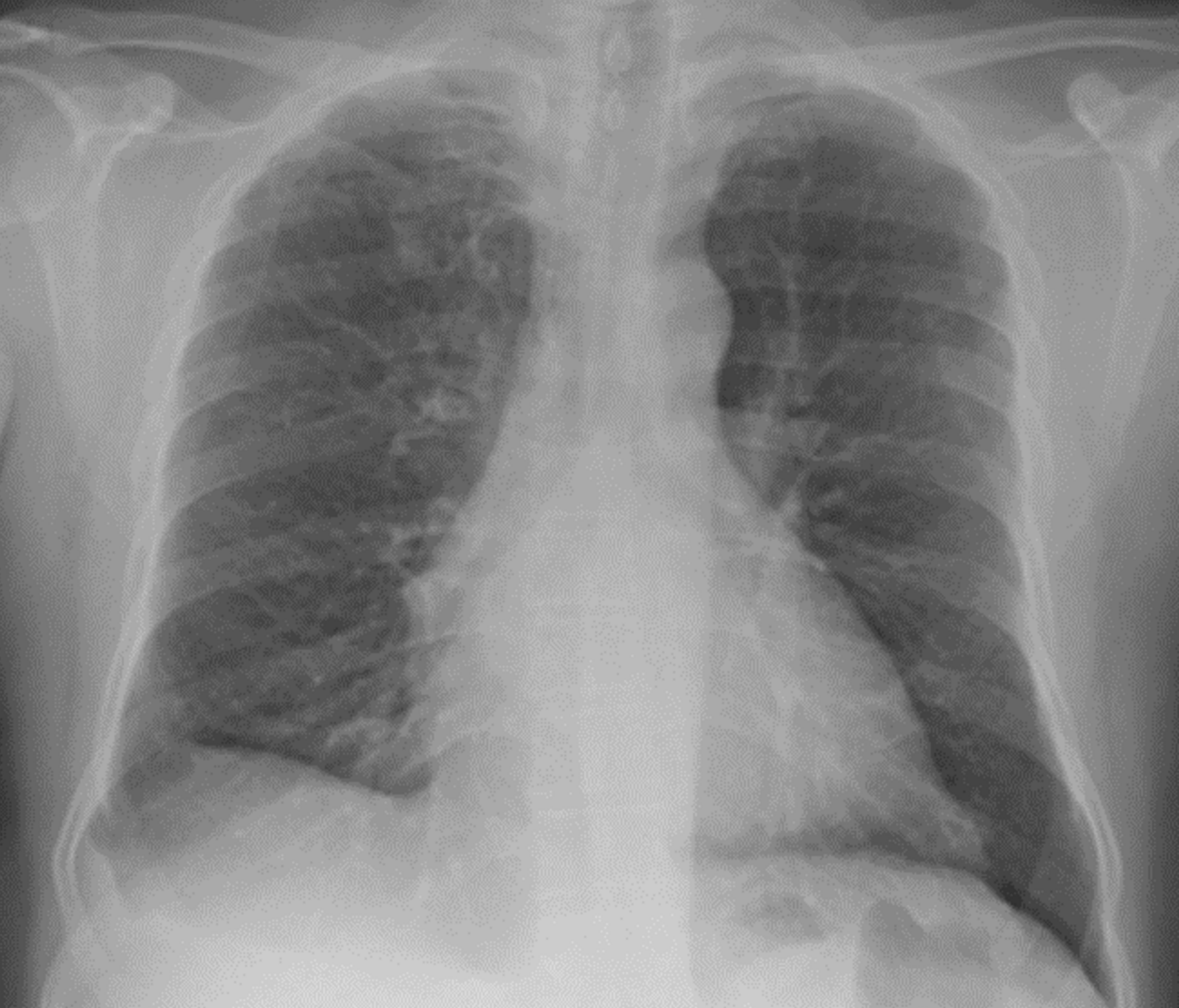
Emphysema

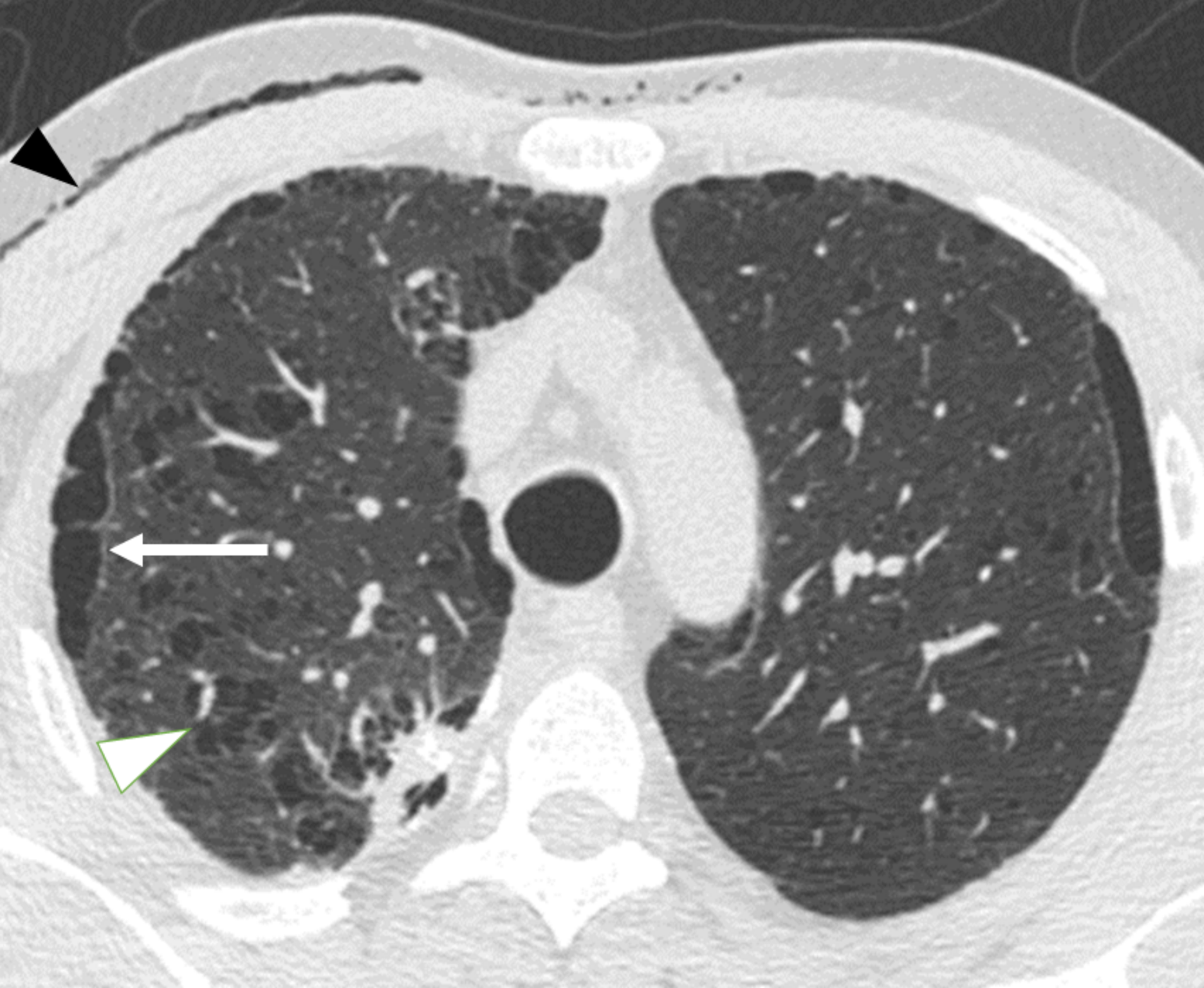
Masses or nodules

Alveolar opacities

Interstitial syndrome









	PSP (n = 44)	SSP (n = 61)	P value
Age (years)	31.2 ± 8.2 [16-51]	44.21 ± 16.7 [18-87]	< 0.005
Sex			0.887
	Male 33/44 (75%)	45/61 (74%)	
	Female 11/44 (25%)	16/61 (26%)	
BMI (Kg/m ²)	20.83 ± 3.6 [15-32]	20.00 ± 3.8 [14-35]	0.302
Smoking habits			0.109
	Active 29/44 (66%)	47/61 (77%)	
	Stop >1year 5/44 (11 %)	9/61 (15%)	
	Non-smoker 10/44 (23%)	5/61 (8%)	
Family history of pneumothorax	0/44 (0%)	6/61 (10%)	0.030
Personal history of pneumothorax	24/44 (55%)	18/61 (30%)	0.015
Surgical treatment	25/44(57%)	32/61 (53%)	0.658
Hospital stay (days)	7.9 ± 9.3 [2-22]	13.2 ± 9.3 [2-36]	<0.001

Quantitative variables are expressed as mean ± SD, numbers in brackets are ranges.

Qualitative variables are expressed as proportions, numbers in parentheses are percentages.

PSP = primary spontaneous pneumothorax; SSP = secondary spontaneous pneumothorax; BMI = body mass index

Bold indicates significant differences

	Chest X-ray	CT (All lesions)	CT (Clinically relevant lesions)
Normal findings	76/105 (72 %)	20/105 (19 %)	43/105 (41 %)
Abnormal findings	29/105 (27 %) (32 lesions)*	85/105 (81 %) (102 lesions)*	62/105 (59%) (71 lesions)*
Emphysema or bullae	23/32 (72%)	76/102 (74.6%)	50/71 (70.4%)
Masse or nodule	5/32 (16 %)	14/102 (13.7%)	11/71 (15.5%)
Alveolar opacity	2/32 (6 %)	4/102 (3.9%)	3/71 (4.2%)
Interstitial syndrome	2/32 (6 %)	8/102 (7.8%)	7/71 (9.9%)

CT = computed tomography. *CT or X-ray may detect more than one lesion

		Chest X-ray		P value
		Abnormal findings	Normal findings	
CT	Normal findings	2/105 (2%)	41/105 (39%)	<0.001
	Abnormal findings	27/105 (26%)	35/105 (33%)	
	Emphysema			
		Present	Absent	
	Emphysema	21/105 (20%)	29/105 (28%)	<0.001
	No emphysema	2/105 (2%)	53/105 (50%)	
	Alveolar opacity			
		Present	Absent	
	Alveolar opacity	1/105 (1%)	2/105 (2%)	<0.001
	No alveolar opacity	1/105 (1%)	101/105 (96%)	
	Mass or nodule			
		Present	Absent	
	Mass/nodule	5/105 (5%)	6/105 (6%)	<0.001
	No mass/nodule	0/105 (0%)	94/105 (89%)	
	Interstitial syndrome			
		Present	Absent	
	Interstitial syndrome	1/105 (1%)	6/105 (7%)	0.014
	No interstitial syndrome	1/105 (1%)	96/105 (91%)	

CT = computed tomography. Bold indicates significant differences

Etiologies

Emphysema	47/61 (77%)
Tuberculosis (active or sequellae)	3/61 (5%)
Lymphangioleiomyomatosis	3/61 (5%)
Lung cancer	2/61 (3%)
Other	6/61 (10%)

<i>Asthma</i>	1
<i>Marfan disease</i>	1
<i>Mesothelioma</i>	1
<i>Desquamative interstitial pneumonia</i>	1
<i>Interstitial pneumonia of unknown origin</i>	1
<i>Cystic pulmonary disease of unknown origin</i>	1