Marta Dąbrowska[1], Anna Kolasa[2], Małgorzata Żukowska[2], Jan Lesiński[1], Joanna Domagała-Kulawik[1], Marta Maskey-Warzęchowska[1], Rafał Krenke[1], Olgierd Rowiński[2], Ryszarda Chazan[1]

[1]Department of Internal Diseases, Pneumology and Allergology, Warsaw Medical University, Poland
Head: prof. R. Chazan, MD, PhD
[2]II[nd] Department of Radiology, Warsaw Medical University, Poland
Head: prof. O. Rowiński, MD, PhD

Analysis of solitary pulmonary nodules found in chest radiograms

Abstract

Introduction: The detection of solitary pulmonary nodules (SPNs) has increased due to widespread use of computed tomography; nevertheless, chest radiographs still remain the basic routine examination.
The aim of the study was to estimate the detection of SPNs in routine chest X-rays in hospitalized patients and to assess the incidence of malignancy in newly diagnosed SPNs.
Material and methods: We analyzed 5726 routine chest radiographs of patients admitted to the Department of Internal Diseases, Pneumology and Allergology in 2004 and 2005. Most of the patients were admitted to hospital due to emergency reasons. The malignant nature of the nodules was confirmed by pathological examination. The nature of benign nodules was confirmed either by pathological examination or based on radiological criteria: no growth within 2 years of radiological follow up, regression in control radiograms or CT scans, benign pattern of calcification.
Results: Among the 5726 radiograms we found 116 newly diagnosed SPNs (2.2%). Twenty-four nodules (21%) were malignant: NSCLC in 21 cases and metastases in 3 cases. Fifty-one nodules (44%) were benign. In 19 patients (16%) SPNs proved to be artefacts or erroneously interpreted extrathoracic lesions. In 22 cases (19%) there was no final diagnosis (lack of data, diagnostic procedure renunciation).
Conclusion: The incidence of newly detected SPNs in chest X-rays was 2.2%. Most SPNs were benign. About 21% of SPNs were diagnosed as malignant.

Key words: solitary pulmonary nodule, chest X-ray, computed tomography of the chest, lung cancer
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Introduction

A solitary pulmonary nodule (SPN) is defined as a focal, oval or round lesion smaller than 3 cm in diameter, which is surrounded by lung parenchyma and is not associated with any other abnormality in the chest radiograph [1]. The differential diagnosis of SPNs includes lesions caused by infection, inflammation, neoplasm (benign or malignant), vascular abnormalities, and congenital malformations. The diagnostic approach and prognosis strongly depend on the nature of SPN and the answer to the question of whether it is benign or malignant in character is crucial. The probability of malignancy may be estimated on the basis of the frequency of malignant SPNs in the given population, the clinical data of the patient (age, smoking history, previous history of cancer), and the radiological appearance of the nodule [2–6].

The frequency of detecting SPN is influenced by the diagnostic method applied and the investigated population. Previous studies have shown that SPNs are found in 0.2% of routine chest radiographs [7–9]. Recent data on this matter are scarce [10]. SPNs are more frequently noted in chest computed tomography [2, 4]; however, conventional chest radiography remains the method of choice in the initial diagnosis of lung diseases.

Address for correspondence: Marta Dąbrowska, MD, Department of Internal Diseases, Pneumology and Allergology, Warsaw Medical University, 1a Banacha St., 02–097 Warsaw, tel.: (+48 22) 599 25 62, fax: (+48 22) 599 15 60, e-mail: mdabrowska@mp.pl

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Table 1. Characteristics of patients with benign and malignant solitary pulmonary nodules

	Malignant nodules n = 24	Benign nodules n = 51
Age (years)	64 (50–82)	69 (41–100)
Sex (female/male)	8/16	25/26
Smoker/Ex-smoker/Non-smoker	5/13/1	8/18/16
Pack-years	30* (0–60)	20* (0–80)
Coincidence of COPD (%)	29	35
Neoplasm in anamnesis (%)	25*	12*
Diameter of nodule [mm]	22* (10–30)	12* (4–30)

*Values are presented as median and range. Statistically significant ($p < 0.05$)

Our study had two objectives: 1) to estimate the frequency of detecting SPNs in routine chest radiographs, and 2) to assess the incidence of malignancy in newly diagnosed SPNs.

Material and methods

The study was a retrospective analysis of routine chest radiographs (CXRs) of patients admitted to the Department of Internal Diseases, Pneumonology and Allergology at Warsaw Medical University in 2004––2005. The CXRs were performed on one of the following three devices: Telemax 1250 (Bennet, USA), Amber N800HF (Odelft, Netherlands), or Philips Digital Diagnost TH/VR (BUF) (Philips, Netherlands).

In 2004 and 2005, 6446 patients were admitted to the above-mentioned department, most of them as emergency conditions. CXRs were performed in 5726 (89%) patients. We selected the radiographs in which focal or oval opacities were described, and of these, we excluded CXRs with other abnormalities (atelectasis, lymphadenopathy), more than one focal lesion, or lesions > 3 cm in diameter. The CXRs of patients admitted to our department for a follow-up of a previously recognized SPN were not taken into consideration (n = 16).

The malignant aetiology of the nodules was confirmed by pathological examination of either post-operative specimens or specimens obtained by transbronchial or transthoracic needle aspiration. The nodules were diagnosed as benign either by pathological sample examination or by radiological follow-up. The radiological criteria for benignity were as follows: presence of calcification (diffuse or central), decrease in dimensions or complete regression of the lesion and lack of growth in a period of at least 2 years of observation [2–4].

The comparative analysis of patients with benign and malignant nodules was performed with the help of the non-parametric Mann-Whitney U-test, $p < 0.05$ being regarded as significant.

Results

From a total of 5726 chest radiographs we found 221 in which round or oval focal lesions were described. Of these, 116 (2.2% of the whole group) met the criteria of SPN as defined above.

The mean age of the patients with SPN was 68 years, there was a slight male predominance (M/F: 64/52). Data on tobacco use were available only in 93 cases: 31 patients had never smoked, 42 were ex-smokers and 20 patients were current smokers. The median number of pack-years for the whole group was 22, in patients with benign nodules smoking history was less relevant than in those with malignant SPNs (20 vs. 30 pack-years, respectively, $p = 0.025$). In the group of patients with malignant nodules only one person (4%) was a never smoker, while benign SPNs occurred in never smokers, ex-smokers, and current smokers as well.

Of the 116 subjects with SPNs, 35 had been diagnosed with chronic obstructive pulmonary disease. Fourteen patients had a history of malignancy (colon cancer = 2, breast cancer = 2, bladder cancer = 2, lung cancer = 2, uterine cervical cancer = 1, prostate cancer = 1, kidney cancer = 1, tongue cancer = 1, ovarian cancer = 1, phaeochromocytoma = 1) (Table 1).

Malignant SPNs were larger than benign (median diameter 22 mm vs. 12 mm, respectively, $p = 0.0001$) and were more frequent in patients with a previous history of cancer and in current and ex-smokers (Table 2).

Malignant nodules were found in 24 patients (24/116, 20.6%). In 21 cases non-small cell lung cancer was diagnosed, and in 3 cases the nodules were identified as metastatic. Benign SPNs were noted in 51 patients, i.e. 43.9% (51/116). In 3 cases the final diagnosis was based on post-operative pathological examination (hamartoma = 1, lymph node = 1, tuberculoma = 1). In the remaining cases, the benign character of the nodule was assumed by radiological

Table 2. Nodule distribution depending on their size

Nodule diameter	Number of nodules	Benign nodules	Malignant nodules	Extrathoracic lesions or artefacts	Nodules without final diagnosis
4–10	42	21	2	11	8
11–20	45	21	9	6	9
21–30	29	9	13	2	5
All	**116**	**51**	**24**	**19**	**22**

criteria. Calcification within the SPNs was present in 19 cases; in 12 subjects no change in the SPNs dimension was observed for at least 2 years of radiological follow-up; a decrease in size or complete regression in control chest radiographs or chest computed tomography was noted in 17 cases.

In 19/116 (16.3%) of the patients SPNs were identified as artefacts or extra-pulmonary lesions. In 3 cases changes described as SPNs proved to be erroneously interpreted shades of nipples. In 16 cases the nodule was not found in control CXR (n = 3) or chest CT (n = 13) performed within 14 days after the first radiograph.

The character of the SPNs was undetermined in 22 patients (22/116, 18.9%). This was due to discontinuation of diagnostic procedures (death of the patient, contraindications associated with the patient's condition, lack of consent, n = 14) or no data on follow-up (n = 8).

Discussion

In our material, SPNs were noted in 2.2% of routine chest radiographs. In the majority of patients, SPNs were benign; malignant nodules accounted for 21% and artefacts for 16% of the analyzed lesions, respectively.

The frequency of detecting SPNs in routine chest radiographs was higher than previously reported. In studies performed 5 decades ago, SPNs were found only in 0.2% of CXRs [7–9]. This difference may result from the method applied and the investigated population. Previous studies concerned CXRs performed as screening for pulmonary tuberculosis, in younger age groups, patients without malignancy, and analyzed small-size radiographs. Our study did not exclude patients who had had a history of neoplastic disease; we also included SPNs with calcifications — both factors could have resulted in a higher incidence of SPNs in our group.

Studies published in the 1980s reported that lung cancer could be detected in 0.30% to 0.68% of conventional chest radiographs in smokers [11, 12]. Assuming that malignant nodules account for about 20% of SPNs seen in chest X-rays, our results are consistent with these findings. The incidence of malignant SPNs in our group was 0.42% (24/5726).

The spectrum of patients admitted to our department does not reflect the general population. Our patients are generally older people, usually smokers, often with a history of chronic respiratory disorder. Therefore, the likelihood of finding an SPNs is higher than in the general population. Patients with COPD (30.2% in our group), a known independent risk factor for lung cancer [13], may serve as an example. It is, however, noteworthy that most of the patients (65%) in our study were hospitalized due to general emergency conditions; patients who were admitted for a follow-up of a previously detected SPNs were not taken into consideration in the analysis. To our knowledge, there are no actual reports on the incidence of SPNs in routine chest radiographs in the Polish population; therefore, a comparative analysis of the results of our study was not possible.

Another factor that might have influenced the incidence of SPNs in our analysis was the development of radiologic imaging techniques. Thanks to digital radiography with image editing, lesions potentially missed in conventional chest imaging are detectable. It is possible to detect a nodule as small as 3 mm; however, in clinical practice SPNs are seldom noted until 5–6 mm in diameter. Small lesions may be hidden in the shade of the mediastinum, diaphragm or the chest wall. Nodules located subpleurally, adjacent to the lung hilus, or in the apex of the lung are poorly visible [14–16]. The detectability of an SPNs depends not only on its size, but also on its density. Consolidated lesions and lesions with calcifications are more easily detected than ground-glass opacities. It has been reported that changes with > 70% area of ground glass are not evident until at least 15 mm in diameter [17]. The detectability of malignant lesions in the lung parenchyma in conventional radiography is three times lower than in computed tomography [18].

Artefacts, defined as SPNs seen in CXR, but not confirmed in CT or control chest radiographs performed within 14 days from the initial investigation, accounted for 16% of the analyzed nodules. This shows the limitations of conventional radiography in detecting SPNs [19]. New (computer-derived) methods of CXR analysis are being elaborated to increase its diagnostic value [20–22], but they have not been introduced to routine clinical practice yet. A high probability of an artefact should be considered when a lesion < 10 mm is found [23]. As our study was a retrospective analysis and the radiographs were evaluated by one radiologist only, the incidence of artefacts may be higher than in prospective studies. The progress in chest imaging, particularly the increasing access to computed tomography, resulted in a higher SPNs detectability. This is an emerging diagnostic problem. In lung cancer screening with low dose CT, SPNs were found in 5 to 50% of patients aged > 45 yrs with a relevant history of smoking [24–27].

In our study, 21% of the nodules found in routine CXRs were malignant and 44% were benign. After excluding the artefacts (19/116), malignant SPNs accounted for 24.7% (24/97), benign for 52.6% (51/97), and indeterminate nodules for 22.7% (22/97) of the detected lesions, respectively. This is consistent with other reports, according to which most SPNs are benign [10].

The radiological criteria of benignity in SPNs diagnosis are the subject of an on-going discussion. Most authors agree that certain types of calcification are typical for benign nodules [3, 4]. The presence and character of calcifications is difficult to evaluate in a conventional radiograph, especially in small nodules, and usually requires confirmation in thin section CT (1.5–3.0 mm section width). Some authors have suggested that small nodules, which are evident in conventional CXRs, are usually calcified [23]; however, the accuracy of evaluating calcifications in this method of chest imaging is low [28]. Central calcifications may also occur in malignant lesions, for example calcified metastases of osteosarcoma [4]. Only 57% (66/116) of our patients had a chest CT; therefore, the evaluation of calcifications within the detected SPNs was difficult. Other features of malignancy: ill-defined, irregular, spicular, or lobulated margins, absence of satellite nodules, are also best evaluated in CT [3, 4]. The widely accepted radiological criterion of stability for at least 2 years of observation as an indicator of SPNs benignity is based on reports from the 1950s and is currently being questioned [9, 29].

Determining the character of an SPNs is a very important clinical issue [1–6, 30, 31]. The probability of malignancy can be estimated by clinical data (age, smoking history, previous malignancy) and the radiological appearance of the nodule (size, margins, the presence of calcifications, structure, and location) [10, 32]. The *a priori* likelihood of SPNs malignancy should also be taken into account [5, 6, 33]. The results of our study may be helpful in the initial analysis of an SPNs detected in the chest radiograph of the hospitalized patient in the Polish population. They provide additional information on the probability of SPNs malignancy, and, together with the clinical history and radiological features of the SPNs, may help in making a decision about further diagnostic approach and management [4–6, 10, 30, 31].

The availability of new methods of chest imaging, dynamic contrast enhanced computed tomography (CECT), single photon emission computed tomography (SPECT), and fluorodeoxyglucose-positron emission tomography (FDG-PET) integrated with CT is increasing. These methods notably improve the diagnostic accuracy of SPNs imaging. CECT and SPECT identify certain benign nodules [34, 35], while FDG-PET/CT indicates malignant lesions [36]. Unfortunately, there are numerous obstacles for introducing PET in routine SPNs evaluation in Poland. The high cost of this technique also limits its wide use.

In conclusion, we have shown that solitary pulmonary nodules are present in up to 2.2% of routine chest radiographs in hospitalized patients. This is a higher incidence than previously reported. Most lesions were benign; malignant SPNs accounted for 21% of the detected nodules.

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