The assessment of the role of baseline low-dose CT scan in patients at high risk of lung cancer

Authors' Contribution:
A Study Design
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Summary

Background: Despite the progress in contemporary medicine comprising diagnostic and therapeutic methods, lung cancer is still one of the biggest health concerns in many countries of the world. The main purpose of the study was to evaluate the detection rate of pulmonary nodules and lung cancer in the initial, helical low-dose CT of the chest as well as the analysis of the relationship between the size and the histopathological character of the detected nodules.

Material/Methods: We retrospectively evaluated 1999 initial, consecutive results of the CT examinations performed within the framework of early lung cancer detection program initiated in Szczecin. The project enrolled persons of both sexes, aged 55–65 years, with at least 20 pack-years of cigarette smoking or current smokers. The analysis included assessment of the number of positive results and the evaluation of the detected nodules in relationship to their size. All of the nodules were classified into I of VI groups and subsequently compared with histopathological type of the neoplastic and nonneoplastic pulmonary lesions.

Results: Pulmonary nodules were detected in 921 (46%) subjects. What is more, malignant lesions as well as lung cancer were significantly, more frequently discovered in the group of asymptomatic nodules of the largest dimension exceeding 15 mm.

Conclusions: The initial, low-dose helical CT of the lungs performed in high risk individuals enables detection of appreciable number of indeterminate pulmonary nodules. In most of the asymptomatic patients with histopathologically proven pulmonary nodules greater than 15 mm, the mentioned lesions are malignant, what warrants further, intensified diagnostics.

Keywords: Lung Cancer • Pulmonary Nodule • Low-Dose CT

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Background

Lung cancer is one of the major health problems in many countries. According to the National Cancer Registry, 140,564 new cases of cancer were reported in Poland in 2010. Lung cancer was the most common type of cancer in males (14,794 new cases) and the second most common type of cancer in females (6038 new cases). In the same year, 92,611 cancer-related deaths were recorded; of

these, most deaths in both males and females were due to to lung cancer (16,187 and 6161 deaths, respectively) [1]. The overall survival of patients with lung cancer is related with the TNM staging of the disease and treatment applied [2–9]. In stage I cancer, 5-year survival is as high as 67% while dropping down to 1–3% for stage IV cancer [9–12]. The average 5-year survival rate in all patients is about 13% [13,14]. The growing scale of the problem and, most of all, high mortality due to lung cancer led to attempts at

the development of an efficient lung cancer screening test. An attempt to use cytological examinations of sputum combined with chest X-rays had failed. No positive correlation between the results of those examinations and the reduction in mortality rates were observed in the studies conducted in the 1970s and 1980s in the US (Johns Hopkins Medical Institutions, Memorial Sloan-Kettering Cancer Center, Mayo Clinic) and Czechoslovakia. [15–23].

As part of the rapid advances in imaging diagnostic techniques in the late 20th century, low-dose computed tomography was developed as an alternative to classical radiography in chest imaging. Published results of the studies conducted by the Japanese group from Nagano, the Japanese Anti-Lung Cancer Association Project and the New York's Early Lung Cancer Action Project opened up opportunities for this diagnostic method to be successfully used in lung cancer screening examinations [22,24–27]. Besides the United states, and Japan, attempts to introduce low-dose CT screening examinations were also made in other countries, such as Belgium, Canada, Denmark, France, Germany, Italy or the Netherlands [22,28]. The first results of randomized trials are quite promising. In the study conducted by the National Cancer Institute in a group of 53,454 subjects, a 20.3% reduction in mortality rates was observed in the group of patients at higher risk of lung cancer subjected to low-dose CT examinations as compared to the group subjected to chest X-ray examinations [29–31]. In Poland, similar projects were started in 2008; multi-directional analysis of results obtained at individual trial sites is ongoing [11].

Material and Methods

Retrospective analysis included the results of 1999 consecutive baseline low-dose CT chest scans performed in one of four diagnostic labs in Szczecin, Poland as part of the early lung cancer detection program. The project recruited individuals at higher risk of lung cancer, both males and females, aged 55 to 65, smoking or with the history of smoking of at least one pack per day for 20 years (pack-years). Individuals who met those criteria received a letter from the Szczecin City Mayor stating the idea of the program and the CT tests as well as providing explanations to potential subjects' concerns. Qualification for the program was made by family physicians who also reported the presence of alarming clinical symptoms, such as cough, shortness of breath, coughing up blood, subfebrile body temperatures, hoarse or dysphagia in a special referral form. Having obtained such referrals, subjects were obliged to report for a CT scan in one of four labs taking part in the program. All test results subject to the assessment were stored in the database of the Screening Test Program Coordination Center.

The analysis of the collected data involved determination of the number of positive results along with the assessment of detected nodular lesions depending on their size. All nodular lesions (including partially calcified lesions) were taken into account, regardless of the percentage content of the solid component and the ground glass component. Completely calcified nodules were treated as benign lesions and excluded from the analysis.

The lesions were classified into the following 6 groups: isolated asymptomatic nodules sized <5 mm (P1), multiple asymptomatic nodules sized <5 mm (P2), isolated asymptomatic nodules sized 5–15 mm (P3), multiple asymptomatic nodules sized 5–15 mm (P4), asymptomatic nodules sized >15 mm (P5), symptomatic nodules sized >15 mm (P6). When lesions of different sizes were detected in a single patient, the size of the largest nodule was decisive in classification. Multiple lesions were defined as the presence of two or more nodules. The analysis included the presence of enlarged mediastinal lymph nodes.

Patients in whom lesions detected in CT scans required further diagnostic management according to the pre-defined algorithm were referred to pneumology centers or to the Clinical Department of Thoracic Surgery of the Pomeranian University of Medicine in Szczecin for more detailed diagnostics. This allowed to isolate the group of patients with confirmed cancer and non-cancer lesions in the lungs. Clinical data including the number and stage of individual cancers as well as the type of detected non-cancer lesions were compared to the analysis of tomographic scan results.

The algorithm used in the program was developed on the basis of the protocols of the International Early Lung Cancer Action Project (I-ELCAP) and the Nelson study and included the following guidelines:
1. Asymptomatic nodules sized <5 mm – follow-up CT scan in 1 year as part of the program (pneumological consultation for more detailed diagnostics in case of multiple nodules).
2. Asymptomatic nodules sized 5–15 mm – attempt of 14-day antibiotic therapy, follow-up CT scan (financed from the National Health Fund) after 3 months for size reassessment. Pneumological consultation in case of progression.. In case of stable or regressing lesions, CT follow-up after 9–12 months as part of the program.
3. Symptomatic or asymptomatic nodules sized >15 mm – pneumological consultation for more detailed diagnostics.

In the following years:
a. Lesion of any size with a growing trend – pneumological consultation for more detailed diagnostics (further management depending on tumor's volume doubling time [VDT]).
b. For lesions stable as compared to the previous scan, see 1 and 2 (possible waiver of repeated antibiotic therapy).

Data subject to the assessment, collected from the diagnostic labs of Independent Public Clinical Hospital No. 1 in Szczecin (HOSPITAL 1), Marie Curie Independent Public Provincial Polyclinical Hospital in Szczecin (HOSPITAL 2) and the Health Care Center of the Ministry of the Interior and Administration in Szczecin (HOSPITAL 3) were recorded between 01 January through 31 December 2010. In case of Prof. Alfred Sokolowski Specialist Hospital in Szczecin-Zdunow (HOSPITAL 4), scans subjected to the analysis were recorded between 01 April through 31 December 2010.

All chest scans were performed without intravenous contrast administrations using two 64-slice Siemens Somatom Sensation Cardiac 64 scanners, one 16-slice Hitachi Eclos 16 scanner and one 6-slice Siemens Somatom Emotion 6 scanner.
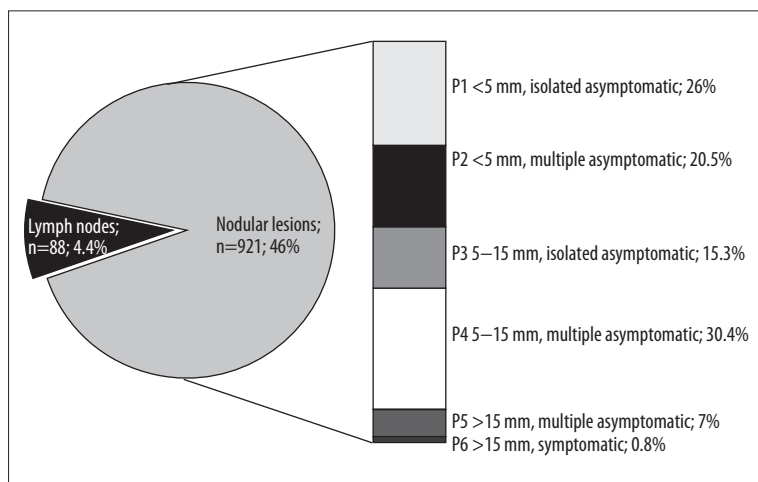
Figure 1. Percentage distribution of the detected lesions in the analyzed group combined with percentage distribution of the nodules with respect to the category they were selected from.
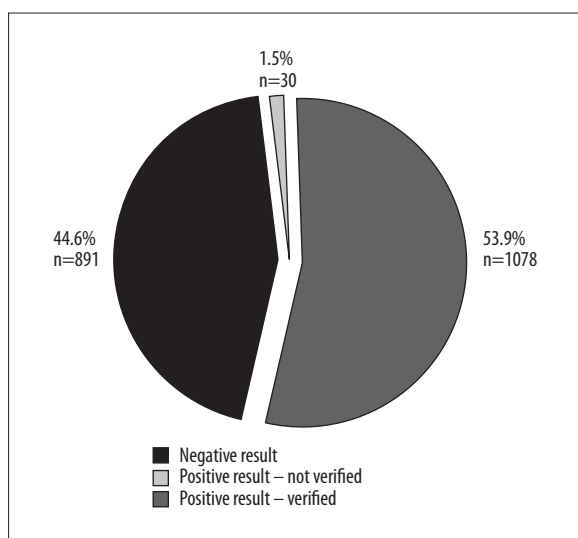

Figure 2. Percentage distribution of the analyzed group with respect to the histopathological verification and examination result.
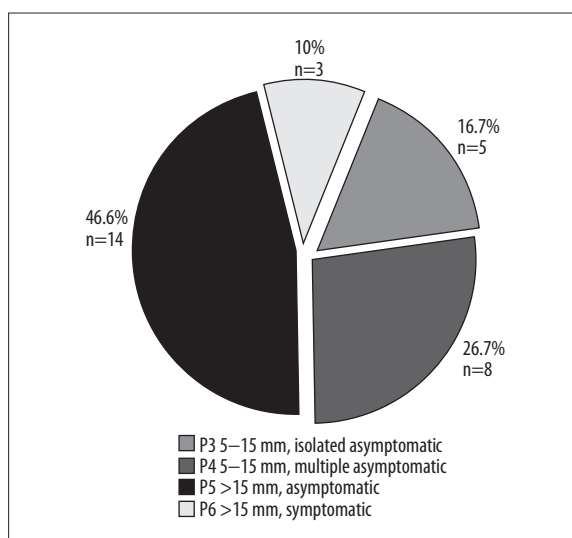

Figure 3. Percentage distribution of the histopathologically verified pulmonary nodules with respect to the category they were selected from.

The scanning parameters approved by the provincial consultant in radiology and applied in two labs were as follows: slice thickness: 5 mm; voltage: 120 kV; current: 17 mAs; CTDIvol: 1.31 mGy. In the remaining labs, acquisition parameters were as follows: slice thickness: 5 mm; voltage: 110 kV; current: 21 mAs; CTDIvol: 1,58 mGy and slice thickness: 5 mm; voltage: 120 kV; current: 40 mAs; CTDIvol: 3.2 mGy.

The statistical analysis of the collected data was conducted using *STATISTICA 10*™ software (StatSoft Inc.) and the following tests: Shapiro-Wilk's W-test, Mann-Whitney's U-test, Fisher's test, Pearson's chi-squared test, Pearson's chi-squared test with Yates' correction. In all tests, statistical significance was defined as $p < 0.05$ while the values between $p = 0.05$ and $p = 0.1$ were considered to be at the border of statistical significance.

Results

The group of subjects qualified to the program of early lung detection of lung cancer using low-dose computed tomography consisted of 1100 females and 899 males (F/M=1.22).

The study group consisted of subjects in the age range of 55–65 years.

The mean age was 59.3 ± 3.03 years (range 55–65). No statistically significant differences were observed in terms of age (p=0.87) or gender (p=0.57) in respective groups. Nodular lesions were detected in 921 (46%) subjects. Negative results were obtained in 1078 (54%) cases. Enlarged lymph nodes were detected in 88 (4.4%) subjects (Figure 1).

The highest numbers of nodular lesions were detected in the categories of asymptomatic lesions sized <5 mm (n=428) (categories P1 and P2) and asymptomatic lesions sized 5–15 mm (n=421) (categories P3 and P4). In group P5 (asymptomatic lesions sized >15 mm) 65 lesions were detected while 7 cases were detected in category P6 (symptomatic lesions sized >15 mm).

In the study group, asymptomatic multiple nodular lesions sized <5 mm were statistically significantly more common in women than in men. No statistically significant correlations between the size of the lesions and the subjects'
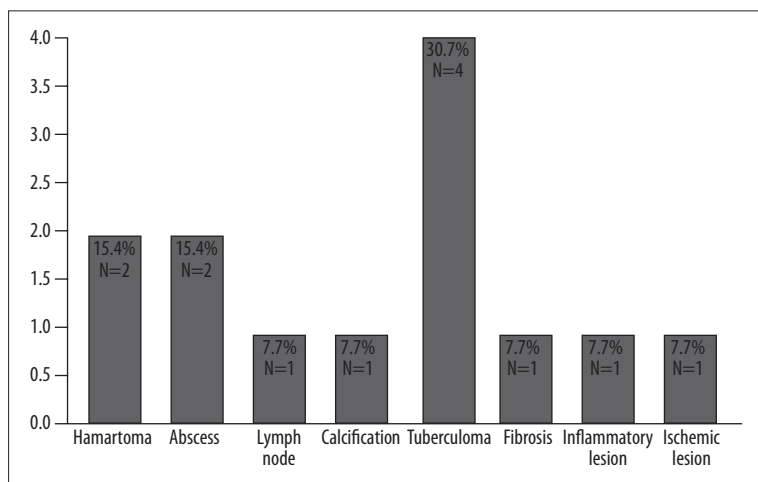
Figure 4. Percentage distribution of the benign lesions with respect to the histopathological diagnosis.
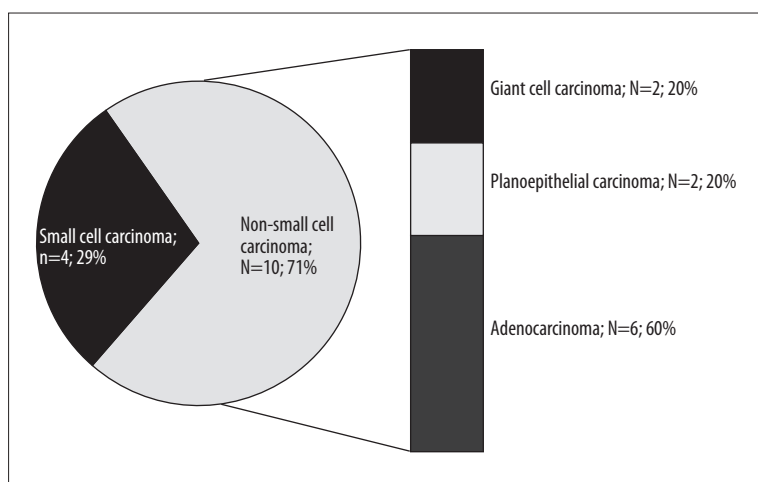

Figure 5. Percentage distribution of the detected lung cancers with respect to their histopathological type.

gender were detected in the remaining groups. Enlarged lymph nodes were statistically significantly more common in males.

Histopathological examination was performed in 30 nodular lesions, accounting for 3% of patients with positive results and 1.5% of the entire study population. Figure 2 presents the percentage distribution of the study population depending on the scan result and histopathological verification, if performed.

Figure 3 illustrates the percentage distribution of histopathologically verified lesions depending on the group of patients from whom the lesions were isolated.

Benign lesions were diagnosed in 43% of histopathologically verified cases (13 out of 30 lesions). Enlarged lymph nodes were detected in 1 case. Figure 4 presents the percentage distribution of benign lesions depending on the histopathological examination result.

In the group of nodular lesions subjected to histopathological examination, 57% of lesions were assessed as malignant (17 out of 30 cases), including 14 cases lung cancer, 1 case of malignant mesothelioma, 1 kidney cancer metastasis and 1 sarcoma metastasis. Lung cancer was confirmed in 82% of histopathologically confirmed cases of malignant lesions (14 out of 17 cases) and in 47% of all verified cases (14 out of 30 cases), accounting for 0.7% of the entire study population.

In the group of histopathologically verified cases, both overall malignant lesions and lung cancer cases were significantly more common in cases of asymptomatic lesions sized >15 mm (p=0.008 and p=0.03, respectively). No statistically significant correlations between the size of the lesions and the nature of neoplastic growth were detected in the remaining groups.

In the group of histopathologically confirmed malignant lung cancers, non-small lung cell carcinoma accounted for 71% of diagnoses (10 out of 14 cases). In the remaining 29% of verified cases (4 out of 14 cases), small lung cell carcinoma was detected. In the group of subjects with confirmed lung cancer, 6 cases (43%) were assessed as clinical stage I, 1 case each (7%) was assessed as clinical stage II and IV, and 6 cases (43%) were assessed as clinical stage III. Figure 5 presents the percentage distribution of diagnosed lung cancers depending on histological type.

In the group of subjects with CT-diagnosed nodular lesions subsequently verified by histopathological examination, inoperable lung cancer was significantly more common in males (p-0.043).
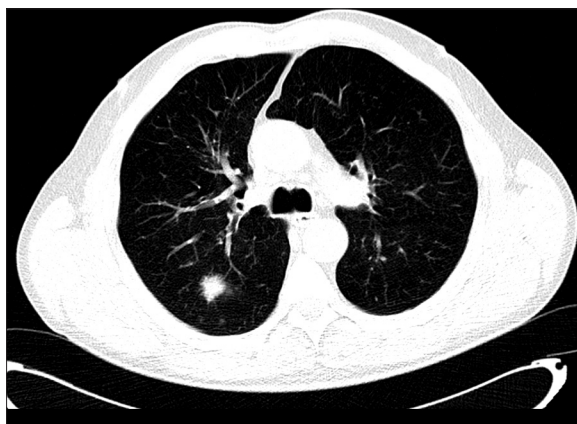
Figure 6. Sarcoma metastasis. Nodule with spiculated margins in 2 segment of the right lung. Category P4 lesion.

Figure 7. Giant cell carcinoma located in the right upper lobe of the lung. Category P5 lesion.

In the group of subjects with histopathologically verified lesions (n=30), enlarged lymph nodes were detected in 7 individuals, including 1 case of enlarged lymph nodes accompanying a benign lesion and 6 cases of enlarged lymph nodes accompanying malignant lesions (Figures 6 and 7).

Discussion

To date, no final conclusions were drawn as pertains the impact of screening tests on the reduced mortality rates in lung cancer; however, the preliminary results appear quite optimistic [29,32–36]. For sure, low-dose computed tomography increases the detection rate of early forms of lung cancer, as confirmed by authors of numerous publications [11,15,24,26,33,37,38]. Also promising are the results of the study conducted by the National Cancer Institute in a group of 53,454 subjects, showing a 20.3% reduction in mortality rates was observed in the group of patients at higher risk of lung cancer subjected to low-dose spiral CT examinations as compared to the group subjected to chest X-ray examinations [29–31,34]. Unfortunately, the preliminary results also suggest numerous problems that have to be addressed before this diagnostic technique is used at larger scale.

At our Szczecin site, 14 cases of lung cancer were detected on the basis of 1999 baseline screening chest scans (0.7%), including 6 cases (43%) diagnosed as clinical stage 1 cancer. The results were submitted to statistical analysis that revealed no significant differences in gender and age with relation to the diagnostic site.

Kaneko et al. published data obtained in the project conducted under the auspices of Anti-Lung Cancer Association (ALCA), involving 3457 low-dose CT scans performed in 1369 patients between September 1993 and April 1995. Fifteen (0.4%) cases of lung cancer were detected, including 14 cases (93%) of stage 1 cancer; the average tumor density was 16 mm [26]. Sone et al. reported that a lung cancer screening program conducted in years 1996-1998 using low-dose computed tomography involved 13786 scans performed in 5483 subjects. Sixty (0.4%) cases of lung cancer were detected, including 55 cases (92%) of stage 1 cancer; the average tumor density was 13.4 mm [26]. Henschke

et al. published the preliminary results of the Early Lung Cancer Action Project (ELCAP), that included 1000 high risk subjects. A total of 27 (2.7%) cancer cases were diagnosed, including 23 (85%) at the earliest stage [20,24,26].

The morbidity rate in the project by Henschke et al. (2.7%) was higher than that observed by the Japanese researchers Kaneko et al. and Sone et al. (0,4%). This might be explained by the differences in the incidence of lung cancer in different countries. Lung cancer is nearly twice as common in the US compared to Japan [26]. However, discrepancies in the results of screening tests may not be always due to epidemiological factors. In a program of early low-dose CT detection of asymptomatic lung cancers conducted in 817 asymptomatic German smokers by Diederich et al., lung cancer was diagnosed in 11 subjects, which corresponded to the morbidity rate of 1.3% [39]. Using an algorithm similar to that proposed by Henschke et al., the authors observed a lower morbidity rate. This appears to be due not only to the age differences between the study groups, but also to the differences in acquisition parameters. Our study does not account for the results of follow-up scans, which makes it impossible to carry out a precise analysis of morbidity in comparison to the literature data.

When analyzing worldwide reports, one may be struck by the lack of unanimity in screening algorithms [24,26,39–42] which with no doubt has an effect on the obtained results. However, it should be kept in mind that examinations using low-dose CT are still in the exploratory phase.

In the results of the cited studies, the percentages of malignant lung tumors detected at clinical stage I was high and ranged from 85% in the ELCAP project to about 90% in the projects conducted by the Japanese researchers [24,26]. At our Szczecin site, 43% of cancers were diagnosed as clinical stage I, and 43% of cancers were diagnosed as clinical stage III between 1 January and 31 December 2010. However, extensive research to identify an optimum screening test have been conducted in the US and Japan for about 40 years [17,19,21,22,23]. In Poland, no large scale attempts to introduce alternative chest imaging forms have been made after cessation of the program of miniature mass X-rays in the 1980s. Therefore, most cases of lung cancers detected in our country are either symptomatic or detected accidentally when performing other diagnostic examinations [11].

Compared to non-European researchers, Diederich et al. observed a decidedly lower percentage of clinical stage I tumors (58%) [39]. Considering the fact that the algorithm used by Diederich et al. was similar to that used in the ELCAP program and that the final report included also the follow-up examinations, this result was not significantly different from the results of our study, considering the fact that only baseline scans were included in our analysis.

In our study, the presence of nodular lesions was demonstrated in 921 (46%) program subjects while also observing that multiple asymptomatic nodules smaller than 5 mm were significantly more common in women. No statistical differences were observed between the age of the subjects and the lesions detected in CT scans. Similar results were obtained by Diederich et al. who observed the presence of nodules in 50% of subjects with to statistically significant differences with regard to subjects' gender and age [39]. The higher incidence of nodules smaller than 5 mm in female subjects might be due to the fact that a higher number of women was enrolled in the program in Szczecin within the period of interest as compared to the number of man (55% *vs.* 45%). The obtained result seems to be of no importance in the aspect of management algorithms being used as the probability of malignancy of nodules smaller than 5 mm is estimated by different authors at about 1% [43,44].

In the Szczecin program, multiple asymptomatic nodular lesions sized 5 to 15 mm were diagnosed in the largest number of participants (n=280). The second most populated group (n=239) was the group of subjects with single asymptomatic nodular lesions not larger than 5 mm. Regardless of the program and percentage ratios, lesions with largest dimensions not exceeding 4 or 5 mm and nodules within the next size category, usually not exceeding 10 mm, constituted the largest groups of study subjects, which appears to be consistent with our observations while ignoring the methodological differences [24,39]. Of note is the fact that individual projects differed in nodule size threshold values [24,39,45]. This is important from the standpoint of the assumed guidelines as management regimens for individual groups of nodules differed largely depending on their size. Larger lesions require more aggressive strategies associated with additional financial demand and increased risk of complications in patients undergoing invasive procedures [43,46]

Another important problem associated with lung cancer screening program guidelines is associated with the determination of the optimum level above which the risk of malignant lesions is significantly elevated. In our study, we observed that in the group subjected to histopathological verification both lung cancer and malignant lesions were statistically more common among asymptomatic nodules larger than 15 mm. It is impossible to overlook discrepancies in data reported in worldwide literature on this subject [24,26,42]. It is however indisputable that the likelihood of malignancy of nodular lesions is directly proportional to their size [43]. Wahidi et al. estimated that the risk of malignancy is 0–1% for lesions sized <5 mm, 6–28% for lesions sized 5–10 mm, 41–64% for lesions sized 1–2 cm and 67–82% for lesions sized 2–3 cm [47,48]. Therefore, in order to meet the primary condition of curing the cancer, i.e. to detect the tumor at the possibly earliest stage, it is legitimate to search for lesions large enough to be resectable and small enough to avoid false positive results.

Unfortunately, due to the population being too small, it was impossible to conduct a reliable analysis of correlations between the nature of lesions and their size in the group of symptomatic patients diagnosed with lesions sized >15 mm. Out of 6 subjects, only 3 could be definitely diagnosed. Other two subjects resigned of further diagnostic tests while one subject suffered severe cerebrocranial injury as a result of traffic accident.

Besides the assessment of size, evaluation of lesion morphology is also important in radiological examinations[44,49–53]. Initially, majority of algorithms used in screening for lung cancer was designed only on the basis of size parameters. Only few authors included structural criteria in their programs [41]. Data obtained in individual screening tests allowed to modify the management algorithm proposed in 2005 by the Fleischner Society, as evidence by guidelines published for example in the US, Japan and France and making diagnostic algorithms dependent on the morphology of lesions [28,54,55].

Introduction of spiral computed tomography led to an increase in the number of small nodular lesions detected in lungs [38,56,57]. Higher sensitivity of this method compared to radiography was documented in numerous articles [2,12,18,21,43,58–60]. Unfortunately, a large part of lesions detected in the scans are of ambiguous clinical nature, and differentiation of benign and malignant lesions remains a challenge for radiologists [32,43,44,56,57,61–64]. In addition, computed tomography is most helpful in detecting peripheral parenchymal nodules, while its usefulness in case of lesions located in direct vicinity of pulmonary hila or within the bronchopulmonary tree is lower and cannot be compared to such diagnostic methods as cytological examination of sputum combined with autofluorescence bronchoscopy [13,31,41]. According to literature data, non-calcified nodules in pulmonary parenchyma are detected in 9-66% of patients, with as much as 88-99% of these lesions being of benign character [65]. Other imaging techniques, such as contrast-enhanced computed tomography, dynamic magnetic resonance imaging and FDG PET proved helpful in differentiating unspecified lung nodules [52,61,63,64,66–69]. However, also these methods are of limited use in evaluating lesions not larger than 10 mm, associated with the largest number of controversies as regards the management algorithms [44,56,57,61–63]. In addition, the value of FDG PET in differentiating ground glass lesions and mixed type lesions is lower than that of solid lesions, and false positive results may be observed in patients with active tuberculosis, histoplasmosis or rheumatic diseases [61].

The lesion volume doubling time is another factor helpful in differentiating benign and malignant nodular lesions [11,49,61,64,65,70]. Benign lesions grow rapidly or very slowly, in contrast to malignant lesions which present an intermediate rate of growth, depending on their histological type [61,64,65,70]. Some authors assume that stability of lesion image over a period of two years suggests its benign character [64,69–71]. However, there are also

supporters of a theory suggesting the need for further follow up of lesions, particularly small nodules of slow growth rate [50,52,56,61,64]. Currently it is assumed that most malignant pulmonary lesions doubles their volume in periods of 20 to 400 days [64]. However, the parameter may have different value depending on the morphology of lesions. Hasegawa et al. observed that the average volume doubling time in case of ground glass, partially solid (mixed) and solid lesions was 813, 457 and 149 days, respectively [43,59,72]. Our study does not account for the results of follow-up examinations, thus making it impossible to assess the rate of lesion growth. However, the primary objective of our analysis was related to the overall data provided by the baseline low-dose chest CT scan.

In screening examinations, assessment of lymph nodes is difficult due to the contrast agent not being administered. With thus-designed protocols, radiologists must keep in minds the anatomical variants that might resemble lymphadenopathy [73]. In our study, enlarged mediastinal lymph nodes were diagnosed in 88 subjects, with the incidence being significantly higher in males. This might be associated with our other observation that inoperable, more advanced stages of cancer were also diagnosed more frequently in males. In addition, on the basis of data analyzed in our study, enlarged lymph nodes were observed in 5 out of 14 subjects with histopathologically confirmed lung cancer. In these 5 patients, only 1 had the tumor at the earliest stage of development. The remaining 4 program participants were diagnosed with lung cancer at clinical stages III and IV. It should be kept in mind that CT scans became the best measure of lymph node volume with significant limitations regarding the analysis of node conditions. The relatively low sensitivity (41–67%) and low specificity (79–86%) of this technique are due to the fact that lymph nodes may be in inflammatory condition, particularly in patients with secondary pneumonia, while lymph nodes of normal size may contain cancer cells [70,71]. Microscopic cancer involvement of normal-size lymph nodes was observed in 5–64% of cases while 15–30% of enlarged lymph nodes were free of cancer cells [70].

When analyzing our program results it should be assumed that following the examination performed as part of the early lung cancer detection program some patients resigned of further diagnostics aimed at elucidation of the nature of their lesions or presented for attempted treatment at another site in Poland. However, considering that the Clinical Department of Thoracic Surgery of the Pomeranian University of Medicine in Szczecin is the only regional center performing lung cancer surgeries and offering its services also to the residents of Lubuskie Province, such likelihood appears to be very low [11].

All examinations, results of which have been presented in this study were carried out in 4 diagnostic labs in Szczecin and subsequently analyzed by different radiologists. Therefore, there is a possibility of discrepancies in the assessments of CT scans provided by different physicians. Leader et al. conducted a study to assess the consistency in the detection of nodular lesions between radiologists analyzing low-dose CT scans [74]. The presented

results demonstrated low degree of consensus between the assessing physicians which, according to the authors, could be corrected by using computer-assisted assessment of CT scans [74,75]. With no doubt, results of the increasing number of papers on Computer Aided Diagnosis (CAD) of nodular lesions require that their widespread use should be considered [31,32,37,43,74–76]. According to some researchers, due to the fact that the assessment of screening tests is much work-consuming, the algorithm should be used as the second, independent assessing entity along with the radiologist [31,75]. This would allow to reduce the number of false negative results [75].

Not all diagnostic labs used identical acquisition parameters. Slight differences were observed mainly in currents, and thus in the volumetric dose index CTDIvol. To date, no consensus has been achieved in relation to minimum clinically acceptable scanning parameters [77], Studies assessing the capabilities of low-dose computed tomography in detection of lung nodules demonstrated that currents in the range of 20–50 mAs were sufficient for the analysis of this type of lesions [77]. This fact was made use of when designing long cancer screening tests; it should be mentioned that the acquisition parameters differed slightly in individual programs [24,39]. Based on the above criteria, it appears that the differences in these parameters should not have a significant impact on the final results of the examinations included in the analysis.

Spiral computed tomography is more sensitive than conventional radiography, and the possibility to use lower exposure doses makes it acceptable from the standpoint of radiological protection in screening tests [21,37,59]. However, only the results of trials assessing the primary endpoint, i.e. the mortality rate shall determine whether the method should be considered most efficient in the early diagnostics of lung cancer [2]. Numerous trials conducted to date revealed a large number of problems that have to be addressed before final decisions can be made [10,32,35,43,52,78,79]. Most controversies are related to the high rate of false positive results, particularly in cases of tiny nodular lesions, leading to unnecessary invasive interventions, excess burden to health care systems and excess costs [32,43,78]. In addition, standardization of diagnostic management algorithms that take into account e.g. financial capabilities of health care systems in individual states, is required [27]. However, one may expect that such a large study group combined with the large amount of data already collected will in near future allow to precisely determine the positive impact of low-dose spiral CT tests on long-term survival.

Conclusions

1. Screening low-dose spiral CT chest scans in patients at high risk of lung cancer allows to detect a significant number of nodular lesion of ambiguous clinical nature.
2. In most asymptomatic patients with lung nodules with diameters larger than 15 mm as revealed in this study and subsequently verified by histopathological examination, the lesions were of malignant character requiring more detailed diagnostic examinations.

References:

1. Wojciechowska U, Didkowska J, Zatoński W: Nowotwory złośliwe w Polsce w 2010 roku. 2012. ISSN 0867-8251 [in Polish]

2. Black WC: Unexpected observations on tumor size and survival in stage IA non-small cell lung cancer. Chest, 2000; 117: 1532–34

3. Chirikos TN, Hazelton T, Tockman M et al: Screening for lung cancer with CT: a preliminary cost-effectiveness analysis. Chest, 2002; 121: 1507–14

4. Flieder DB, Port JL, Korst RJ et al: Tumor size is a determinant of stage distribution in t1 non-small cell lung cancer. Chest, 2005; 128: 2304–8

5. Janssen-Heijnen MLG, Coebergh JWW: Trends in incidence and prognosis of the histological sybtypes of lung cancer in North America, Australia, New Zealand and Europe. Lung Cancer, 2001; 31: 123–37

6. Port JL, Kent MS, Korst RJ et al: Tumor size predicts survival within stage IA non-small cell lung cancer. Chest, 2003; 124: 1828–33

7. Wisnivesky JP, Yankelevitz D, Henschke CI: Stage of lung cancer in relation to its size: part 2. Evidence. Chest, 2005; 127: 1136–39

8. Wisnivesky JP, Yankelevitz D, Henschke I: The effect of tumor size on curability of stage I non-small cell lung cancers. Chest, 2004; 126: 761–65

9. Xiong Z, Xiong G, Man Y et al: Detection of lung cancer by oral examination. Medical Hypotheses, 2010; 74: 346–47

10. Getman VV, Mueller MR: Epidemiology (incidence, survival), risk factors, prevention (screening). Eur Surg, 2004; 36: 61–65

11. Grodzki T, Walecka A, Fabian W et al: Program wczesnego wykrywania nowotworów płuc za pomocą tomografii komputerowej – wstępne doświadczenia Szczecina. Pneumonol Alergol Pol, 2009; 77: 521–27 [in Polish]

12. Swensen SJ, Jett JR, Hartman TE et al: Lung cancer screening with CT: Mayo Clinic experience. Radiology, 2003; 226: 756–61

13. Lam B, Lam SY, Wong MP et al: Sputum cytology examination followed by autofluorescence bronchoscopy: A practical way of identifying early stage lung cancer in central airway. Lung Cancer, 2009; 64: 289–94

14. Ruano-Ravina A, Figueiras A, Barros-Dios JM: Lung cancer and related risk factors: an update of the literature. Public Health, 2003; 117: 149–56

15. Bach PB, Kelley MJ, Tate RC et al: Screening for lung cancer: a review of the current literature. Chest, 2003;123(1 Suppl.): 72S–82S

16. Bach PB, Silvestri GA, Hanger M et al: Screening for lung cancer: ACCP evidence-based clinical practice guidelines (2nd ed.). Chest, 2007; 132(3 Suppl.): 69S–77S

17. Doria-Rose VP, Marcus PM, Szabo E et al: Randomized controlled trials of the efficacy of lung cancer screening by sputum cytology revisited: a combined mortality analysis from the Johns Hopkins Lung Project and the Memorial Sloan-Kettering Lung Study. Cancer, 2009; 115: 5007–17

18. Dziadziuszko R: Leczenie drobnokomórkowego raka płuca – zalecenia European Society for Medical Oncology (ESMO) z 2010 roku. Med Prakt, 2012; (1): 73–76 [in Polish]

19. Melamed MR, Flehinger BJ, Zaman MB et al: Screening for early lung cancer. Results of the Memorial Sloan-Kettering study in New York. Chest, 1984; 86: 44–53

20. Rossi A, Maione P, Colantuoni G et al: Screening for lung cancer: New horizons? Crit Rev Oncol Hematol, 2005; 56: 311–20

21. Roszkowski K: Komentarz do artykułu T. Grodzkiego i wsp. "Program wczesnego wykrywania nowotworów płuc za pomocą tomografii komputerowej – wstępne doświadczenia Szczecina". Pneumonol Alergol Pol, 2009; 77: 571–72 [in Polish]

22. Sagawa M, Usuda K, Aikawa H et al: Lung cancer screening and its efficacy. Gen Thorac Cardiovasc Surg, 2009; 57: 519–27

23. Sanderson DR: Lung cancer screening: the Mayo study. Chest, 1986; 89: 324S

24. Henschke CI, McCauley DI, Yankelevitz DF et al: Early Lung Cancer Action Project: overall design and findings from baseline screening. Lancet, 1999; 354: 99–105

25. Mazzone PJ: Lung cancer screening: an update, discussion, and look ahead. Curr Oncol Rep, 2010; 12: 226–34

26. Sobue T, Moriyama N, Kaneko M et al.: Screening for lung cancer with low-dose helical computed tomography: Anti-Lung Cancer Association Project. J Clin Oncol, 2002; 20: 911–20

27. Wisnivesky JP, Mushlin AI, Sicherman N et al: The cost-effectiveness of low-dose CT screening for lung cancer: preliminary results of baseline screening. Chest, 2003; 124: 614–21

28. Couraud S, Cortot AB, Greillier L et al: From randomized trials to the clinic: is it time to implement individual lung-cancer screening in clinical practice? A multidisciplinary statement from French experts on behalf of the french intergroup (IFCT) and the groupe d'Oncologie de langue française (GOLF). Ann Oncol, 2013; 24: 586–97

29. Aberle DR, Adams AM, Berg CD et al: Reduced lung-cancer mortality with low-dose computed tomographic screening. N Engl J Med, 2011; 395–409

30. Statement concerning the National Lung Screening Trial [online].2008.[dostęp: 02 marca 2012].Dostępny w Internecie: *http://www.cancer.gov/images/dsmb-nlst.pdf*

31. White CS.: National Lung Screening Trial: a breakthrough in lung cancer screening? J Thorac Imaging, 2011; 26: 86–87

32. Boiselle PM, Ernst A, Karp DD: Lung cancer detection in the 21st century: potential contributions and challenges of emerging technologies. Am J Roentgenol, 2000; 175: 1215–21

33. Jett JR, Midthun DE: Screening for lung cancer: current status and future directions: Thomas A. Neff lecture. Chest, 2004; 125 (5 Suppl.): 158S–62S

34. Mulshine JL, van Klaveren RJ: Lung cancer screening: what is the benefit and what do we do about it? Lung Cancer, 2011; 71: 247–48

35. Ravenel JG, Costello P, Silvestri GA: Screening for lung cancer. Am J Roentgenol, 2008; 190: 755–61

36. Warner E, Jotkowitz A, Maimon N: Lung cancer screening-are we there yet? Eur J Intern Med, 2010; 21: 6–11

37. Diederich S, Wormanns D: Impact of low-dose CT on lung cancer screening. Lung Cancer, 2004; 45 (Suppl.2): S13–19

38. Ganti AK, Mulshine JL: Lung cancer screening. Oncologist, 2006; 11: 481–87

39. Diederich S, Wormanns D, Semik M et al: Screening for early lung cancer with low-dose spiral CT: prevalence in 817 asymptomatic smokers. Radiology, 2002; 222: 773–81

40. Lopes Pegna A, Picozzi G, Mascalchi M et al: Design, recruitment and baseline results of the ITALUNG trial for lung cancer screening with low-dose CT. Lung Cancer, 2009; 64: 34–40

41. Menezes RJ, Roberts HC, Paul NS et al: Lung cancer screening using low-dose computed tomography in at-risk individuals: the Toronto experience. Lung Cancer, 2010; 67: 177–83

42. Nawa T, Nakagawa T, Kusano S et al: Lung cancer screening using low-dose spiral CT: results of baseline and 1-year follow-up studies. Chest, 2002; 122: 15–20

43. MacMahon H, Austin JH, Gamsu G et al: Guidelines for management of small pulmonary nodules detected on CT scans: a statement from the Fleischner Society. Radiology, 2005; 237: 395–400

44. Xu DM, van der Zaag-Loonen HJ, Oudkerk M et al: Smooth or attached solid indeterminate nodules detected at baseline CT screening in the NELSON study: cancer risk during 1 year of follow-up. Radiology, 2009; 250: 264–72

45. Swensen SJ: CT screening for lung cancer. Am J Roentgenol, 2002; 179: 833–56

46. Alberts WM: Diagnosis and management of lung cancer executive summary: ACCP evidence-based clinical practice guidelines (2nd ed.). Chest, 2007; 132(3 Suppl.): 1S–19S

47. Austin JH: The incidental small pulmonary nodule and the Fleischner criteria 5 years later: have we learned anything more? J Thorac Imaging, 2011; 26: 88–89

48. Brandman S, Ko JP: Pulmonary nodule detection, characterization, and management with multidetector computed tomography. J Thorac Imaging, 2011; 26: 90–105

49. Libby DM, Smith JP, Altorki NK et al: Managing the small pulmonary nodule discovered by CT. Chest, 2004; 125: 1522–29

50. Ohta Y, Shimizu Y, Kobayashi T et al: Pathologic and biological assessment of lung tumors showing ground- glass opacity. Ann Thorac Surg, 2006; 81: 1194–98

51. Henschke CI, Yankelevitz DF, Mirtcheva R et al: CT screening for lung cancer: frequency and significance of part-solid and nonsolid nodules. Am J Roentgenol, 2002; 178: 1053–57

52. Wahidi MM, Govert JA, Goudar RK et al: Evidence for the treatment of patients with pulmonary nodules: when is it lung cancer?: ACCP evidence-based clinical practice guidelines (2nd ed.). Chest, 2007; 132 (3 Suppl.): 94S–107S

53. Lee HY, Lee KS: Ground-glass opacity nodules: histopathology, imaging evaluation, and clinical implications. J Thorac Imaging, 2011; 26: 106–18

54. Jacobson FL, Austin JHM, Field JK et al: Development of The American Association for Thoracic Surgery guidelines for low-dose computed tomography scans to screen for lung cancer in North America: Recommendations of The American Association for Thoracic Surgery Task Force for Lung Cancer Screening and Surveillance. J Thorac Cardiovasc Surg, 2012; 144: 25–32

55. Guidelines for the management of pulmonary nodules detected by low-dose CT lung cancer screening [online]. 2013. [Access: 23 November 2013]. *http://jscts.org/pdf/guideline/gls3rd_english130621.pdf.*

56. Benjamin MS, Drucker EA, McLoud TC et al: Small pulmonary nodules: detection at chest CT and outcome. Radiology, 2003; 226: 489–93

57. Jeudy J, White CS, Munden RF et al: Management of small (3–5-mm) pulmonary nodules at chest CT: global survey of thoracic radiologists. Radiology, 2008; 247: 847–53

58. Erasmus JJ, Connolly JE, McAdams HP et al: Solitary pulmonary nodules: Part I. Morphologic evaluation for differentiation of benign and malignant lesions. Radiographics, 2000; 20: 43–58

59. Li F, Sone S, Abe H et al: Low-dose computed tomography screening for lung cancer in a general population: characteristics of cancer in non-smokers versus smokers. Acad Radiol, 2003; 10: 1013–20

60. Strauss GM., Dominioni L, Jett J.R., et al.: Como international conference position statement: lung cancer screening for early diagnosis 5 years after the 1998 Varese conference. Chest 2005;127: 1146–51

61. Erasmus JJ, McAdams HP, Connolly JE: Solitary pulmonary nodules: Part II. Evaluation of the indeterminate nodule. Radiographics, 2000; 20: 59–66

62. Markowitz SB, Miller A, Miller J et al: Ability of low-dose helical CT to distinguish between benign and malignant noncalcified lung nodules. Chest, 2007; 131: 1028–34

63. Schaefer JF, Vollmar J, Schick F et al: Solitary pulmonary nodules: dynamic contrast-enhanced MR imaging-perfusion differences in malignant and benign lesions. Radiology, 2004; 232: 544–53

64. Yankelevitz DF, Henschke CI: Does 2-year stability imply that pulmonary nodules are benign? Am J Roentgenol, 1997; 168: 325–28

65. Takashima S, Sone S, Li F et al: Indeterminate solitary pulmonary nodules revealed at population- based CT screening of the lung: using first follow- up diagnostic CT to differentiate benign and malignant lesions. Am J Roentgenol, 2003; 180: 1255–63

66. Lowe VJ, Fletcher JW, Gobar L et al: Prospective investigation of positron emission tomography in lung nodules. J Clin Oncol, 1998; 16: 1075–84

67. Silva CT, Amaral J, Moineddin R et al: CT characteristics of lung nodules present at diagnosis of extrapulmonary malignancy in children. Am J Roentgenol, 2010; 194: 772–78

68. Swensen SJ, Brown LR, Colby TV et al: Pulmonary nodules: CT evaluation of enhancement with iodinated contrast material. Radiology, 1995; 194: 393–98

69. Takashima S, Sone S, Li F et al: Small solitary pulmonary nodules (≤1 cm) detected at population-based CT screening for lung cancer: reliable high-resolution CT features of benign lesions. Am J Roentgenol, 2003; 180: 955–64

70. Prokop M, Galanski M: Spiralna i wielorzędowa tomografia komputerowa człowieka. 2007. ISBN 978-83-89769-23-7 [in Polish]

71. Webb WR: Radiologic evaluation of the solitary pulmonary nodule. Am J Roentgenol, 1990; 154: 701–8

72. Hasegawa M, Sone S, Takashima S et al: Growth rate of small lung cancers detected on mass CT screening. Br J Radiol, 2000; 73: 1252–59

73. Glazer HS, Aronberg DJ, Sagel SS: Pitfalls in CT recognition of mediastinal lymphadenopathy. Am J Roentgenol, 1985; 144: 267–74

74. Leader JK, Warfel TE, Fuhrman CR et al: Pulmonary nodule detection with low-dose CT of the lung: agreement among radiologists. Am J Roentgenol, 2005; 185: 973–78

75. Das M, Mühlenbruch G, Heinen S et al: Performance evaluation of a computer-aided detection algorithm for solid pulmonary nodules in low-dose and standard-dose MDCT chest examinations and its influence on radiologists. Br J Radiol, 2008; 81: 841–47

76. Oda S, Awai K, Murao K et al: Computer-aided volumetry of pulmonary nodules exhibiting ground-glass opacity at MDCT. Am J Roentgenol, 2010; 194: 398–406

77. Kubo T, Lin P-J P, Stiller W et al: Radiation dose reduction in chest CT: a review. Am J Roentgenol, 2008; 190: 335–43

78. Lee CI, Forman HP: CT screening for lung cancer: implications on social responsibility. Am J Roentgenol, 2007; 188: 297–98

79. Parkin DM, Moss SM: Lung cancer screening: improved survival but no reduction in deaths – the role of " overdiagnosis". Cancer, 2000; 89: 2369–76