CLINICAL AND RADIOLOGICAL MANIFESTATIONS OF ASBESTOSIS DEPENDING ON THE MINERALOGIC CHARACTERISTICS OF ASBESTOS

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SUMMARY - Dependence of the incidence of pulmonary/pleural asbestosis on the mineralogic characteristics of asbestos, and sensitivity of chest roentgenogram and high-resolution computed tomography on analyzing this pathology are presented. This retrospective/prospective study was conducted in 109 patients, workers of Plobest Ltd Asbestos Industry in Ploče (group 1, predominantly inhaling chrysotile asbestos) and 216 workers of Salonit Ltd from Vranjic near Split and Split Shipyard (group 2, predominantly inhaling crocidolite asbestos) with the diagnosis of pulmonary/ pleural asbestosis. Statistical analysis was done by Kappa test, χ^2 -test, and analysis of variance. Test results are shown in diagrams and table. Pulmonary asbestosis was confirmed in 38 (35%), pulmonary and pleural asbestosis in 49 (45%), and pleural asbestosis in 22 (20%) group 1 patients (exposed to chrysotile). In group 2 patients (exposed to crocidolite asbestos), pulmonary asbestosis was confirmed in only 9 (4%), pleural asbestosis in 117 (54%), and pleural and pulmonary asbestosis in 90 (42%) patients. In 35 (32.1%) group 1 patients with normal chest roentgenograms (International Labour Organisation (ILO) perfusion categories 0/0 and 0/1), high-resoluton computed tomography revealed initial or moderate stage of interstitial pulmonary fibrosis. Interpretation of chest roentgenograms showed good, almost excellent agreement between the results obtained by three observers on ILO profusion categories 0/0, 0/1 and 1/0, and "normal" agreement for profusion category $\geq 1/1$. For pleural asbestosis, two readers had excellent agreement (Kappa test = 79%) in group 1 and good agreement in group 2. It was concluded that the incidence of pulmonary and pleural asbestosis was much higher in persons exposed to the inhalation of chrysotile and crocidolite, respectively. It is recommended that in radiologic diagnosis, high-resolution computed tomography should always be used in addition to ILO classification, particularly in the initial stages of the lung and pleural disease.

Introduction

Benign asbestosis is a pulmonary and/or pleural fibrosing disease caused by inhalation of asbestos particles or fibers. Clinical diagnosis is based on radiologic examinations and confirmed exposure to asbestos, with a reasonably long latency period between the initial exposure and disease detection. The principal radiologic method of examination is plain thoracic x-ray performed under exactly determined technical conditions specified in the International Labour Organisation (ILO) recommendations for pneumoconioses¹. Regardless of the fact that the ILO classification is generally accepted, this system is insufficient and lacks precision². This particularly holds for the pleural form of benign asbestosis where variability in the interpretation of findings of the same chest roentgenograms is sig-

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nificant³. In addition to this traditional method, a revolutionary advancement of computer technology in the field of radiology has made chest computed tomography (CT) an unavoidable method in diagnosing these diseases in the last 20 years. Chest CT, particularly high-resolution computed tomography (HRCT), shows high sensitivity to pathomorphologic changes in the chest caused by asbestos exposure. According to literature data, 10%-50% of asbestosis-affected individuals have normal chest x-ray and pathologic HRCT findings⁴⁻⁶.

The pathophysiologic mechanisms of this non-malignant pneumoconiosis are not fully known. The inhaled asbestos particles and fibers are in part removed by respiration, and in part are deposited in various ways in different anatomical regions of the respiratory system⁷. The deposited asbestos particles are cytotoxic, so the activation of inflammatory cells and other as yet insufficiently studied complex mechanisms induce damage to the pulmonary tissue⁸. Since pleural plaques most often occur at the sites of largest pleural movement on breathing, it is assumed that the airborne asbestos fibers transported by breathing motions penetrate the visceral pleura and cause microhemorrhage and fibrin depositions in parietal pleura^{9,10}. Studies correlating mineralogic characteristics and size of asbestos particles with different clinical forms of benign asbestos-related disease are rare. The predominant research topic is the relation between the mineralogic characteristics of inhaled asbestos and increased risk of mesothelioma and lung cancer¹¹⁻¹⁶.

The purpose of this paper is to report on the incidence of different forms of benign asbestos-related diseases (pulmonary and/or pleural asbestosis) in dependence on mineralogic characteristics of inhaled asbestos, and to analyze diagnostic reliability of radiologic methods in the diagnosis of asbestos-related diseases.

Patients and Methods

This retrospective/prospective study included 109 patients, workers of Plobest Ltd. Asbestos Industry from Ploče (group 1, predominantly inhaling chrysotile asbestos) and 216 workers of Salonit Ltd from Vranjic near Split and Split Shipyard (group 2, predominantly inhaling crocidolite asbestos) with the diagnosis of pulmonary/ pleural asbestosis. Sex and age distribution of patients is given in Fig. 1. All study patients underwent necessary occupational medical examinations, functional pulmonary examinations, pulmonologist's examinations and radio-

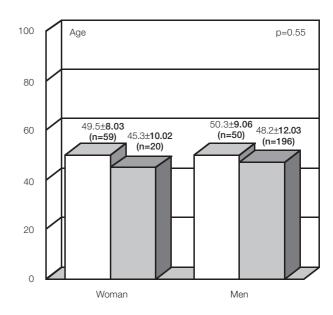
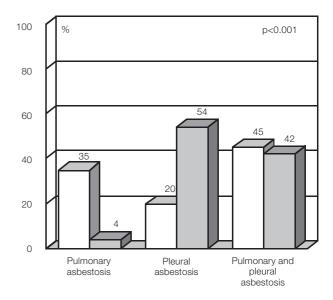


Fig. 1. Patient distribution according to sex, age and asbestos type.

Fig. 2. Types of asbestosis according to patient exposure to different types of asbestos.



logic tests. Posteroanterior (PA) and lateral chest x-rays at 45° with deep inspiration were obtained. The distance between the focus and film on taking x-rays was 180 cm, electrical characteristics 130 kV, 3-5 mAs, and exposition time 0.4 seconds. All radiographs were independently interpreted by three radiologists who used ILO-set of radiographs published by the International Labour Organisation (ILO set). The results identically interpreted

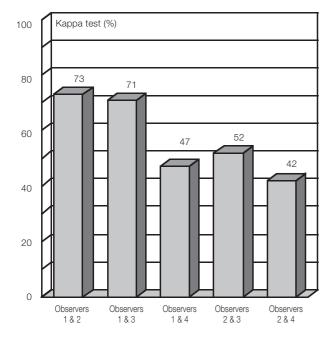


Fig. 3. Interobserver agreement of ILO categories of profusion for parenchymal small opacities on chest radiography.

by at least two observers were taken for consideration. When the discrepancy between the findings from ILO patterns was higher, the chest films were additionally interpreted by a forensic radiology expert, or chest HRCT was performed. The scanning was performed in 55 (50.5%) patients from group 1. HRCT was performed on a fourth generation Somatom DRG (Siemens) equipment, soon after standard radiology (up to 1 month). A small number of patients were scanned on a spiral CT Somatom Emotion (Siemens) of the new generation. In all cases the scanning started from lung apexes to the lung bases at 5-12 levels, with slice thickness of 1-1.5 mm. The examination was conducted in supine position with deep inspiration, and additional scans were made in prone position when changes in the pulmonary interspace were suspected. The scanning was conducted on a Somatom DRG (voltage 130 kV, current 180-300 mA, scanning time 3.4 seconds) and spiral CT (voltage 130 kV, current 100 mA, scanning time 0.8 seconds). The scanned sections were photographed in three typical "windows" for (a) pulmonary tissue, (b) pleura, and (c) pulmonary tissue and pleura. Statistical analysis was done by Kappa test, c²-test, and analysis of variance. Test results are shown in diagrams and table.

Results

The incidence of different types of benign asbestosis is shown in Fig. 2. As seen from Fig. 2, the group of patients exposed to chrysotile included 38 (35%) patients with pulmonary asbestosis, whereas the group exposed to crocidolite asbestos included a considerably greater proportion of pleural asbestosis patients, i.e. 117 (54%). The difference is statistically significant (c^2 =66.7; p<0.001).

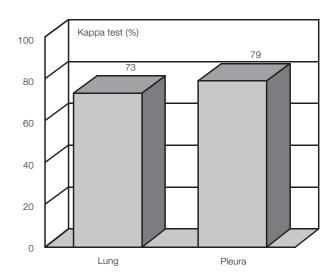
The degree of agreement of the observers' findings interpreting the changes on the same chest films is shown in Fig. 3. So, a high, almost excellent agreement was recorded between observers 1 and 2, and observers 1 and 3. Kappa test yielded good agreement between observers 1 and 4, 2 and 3, and 2 and 4. The agreement between observers 1 and 2 on pulmonary and pleural asbestosis is shown in Fig. 3.

Figure 4 shows good, almost identical interpretation of lung asbestosis, and excellent agreement on pleural asbestosis between observers 1 and 2 (>75%).

In group 1 with pulmonary/pleural asbestosis, the diagnosis was definitely verified by HRCT in as many as 35 (32.1%) patients (Table 1).

According to data from Table 1, interstitial pulmonary fibrosis related to asbestos inhalation was determined by CT in ten patients with normal chest radiography results (ILO profusion categories 0/0 and 0/1), whereas three patients were excluded. In the group of 25 patients with chest x-ray findings suspect for asbestosis (ILO categories 0/1 and 1/0; 3 independent ILO classifications), HRCT indicated mild fibrosis in 20 and moderate fibro-

Fig. 4. Observer 1 and 2 agreement for lung and pleural asbestosis.



Chest radiography	No. of patients	HRCT: lung fibrosis		
(ILO categories)		mild	moderate	none
0/0, 0/1	13	10	0	3
0/1, 1/0	25	20	5	0
≥1/1	17	5	12	0
Total	55	35	17	3

Table 1. Correlation between chest x-ray by ILO classification and high-resolution computed tomography (HRCT).

sis in five patients. In the group of 17 patients with confirmed radiologic signs of fibrosis on chest roentgenograms (ILO categories $\geq 1/1$), HRCT confirmed interstitial pulmonary fibrosis in all cases.

Discussion

Pleural plaque and lung fibrosis are the most common manifestations of asbestos-related diseases. However, the pathogenesis of these pleural and lung asbestos-induced injuries is poorly understood. Both chrysotile and crocidolite exposure induces persistent macrophage inflammatory response within the pleural space, and these fibers can act synergistically with interleukin-1 beta in stimulating the formation of nitric oxide by pleural mesothelial cells.

Chrysotile is presently a dominant form of asbestos used in international commerce. Chrysotile fibers are made up of bundles of fibrils, usually exhibiting a curved and twisted morphology in air samples, and are relatively easily separated into fine, flexible bundles¹⁶. Natural fiber length varies between 1 and 40 μ m, and fiber diameter varies between 0.01 and 1 mm. In inhalation studies in rats, chrysotile, was found to be much more readily eliminated from the lungs than crocidolite^{17,18}.

The amphibole asbestos, crocidolite, differs from chrysotile in containing more silica, iron, sodium and calcium oxide, and less magnesium oxide and water. Crocidolite fibers are generally straight and longer¹⁹. Crocidolite fibers are much more harmful than chrysotile fibers11. Comparative analyses have established that chrysotile is 2 to 4 times less potent than crocidolite asbestos in its ability to cause malignant mesothelioma, but is equally potent in causing lung cancer²⁰.

The results of our study indicated a statistically significant difference between these two types of asbestos in clinical and radiologic manifestations of asbestosis. In the group of patients exposed to chrysotile inhalation for years (group 1), the incidence of pulmonary asbestosis was considerably higher than that of pleural asbestosis. The results were inverse for group 2 patients predominantly exposed to the inhalation of crocidolite asbestos. They were mostly affected by pleural asbestosis, with pulmonary asbestosis in 4% of cases only. The results of our study almost completely agree with those of Blažić, obtained by 20-year follow-up of the Pula Shipyard workers²¹. Similar results are reported by Poretti, based on his long-time follow-up and mineralogic analyses of asbestos²². The possible causes of variable clinical manifestations of asbestosis include difference in fiber size^{13,23,24} and even more the greater exposure to these fibers²⁵.

The primary radiologic procedure for determination of asbestosis is plain chest film (oblique and lateral projections) performed under strictly defined and repeatable conditions.

The pulmonary form of the disease is connected with interstitial pulmonary fibrosis (non-specific), visualized on roentgenogram as irregular linear and reticular shadows in the marginal parts of the lung bases, mostly posteriorly, and in the central lung regions. Other radiologic signs of asbestosis include circumscribed pleural plaques (with/ without calcifications), diffuse pleural thickenings (unilateral/bilateral) of different width and length, adhesions of f.c. sinuses, and rarely round subpleural atelectasis (pseudotumor shadows). Lung fibrosis can occur alone, without pleural plaques, or as diffuse pleural thickening, and vice versa.

Although the clinical practice has generally adopted ILO classification with minor changes and amendments (limited in extent) in the national public health systems, this asbestosis classification system has its limitations and inadequacies. This is particularly true for pleural asbestosis, since ILO classification is not precise and reliable enough for such changes, and there is a significant percentage of false positive and a smaller percentage of false negative findings. Thus, e.g., plain x-rays do not allow for differentiation of the extrapleural fat tissue (normal physiologic and anatomic phenomenon, particularly in persons with increased body weight) from fibrous pleural thickening caused by inhalation of asbestos, or differentiation of a large pleural plaque from diffuse pleural thickening²⁶.

Correct interpretation of the changes visualized on plain chest films, particularly of diffuse changes in lung tissue, is one of the major and most frequently encountered problems in diagnostic radiology⁵. The reasons are myriad: most of the pulmonary diseases simultaneously involve the interstitium and alveolar lung space, the level of involvement depending on the disease and its severity, patient, timing of radiologic examination, and the like. Further, the method has technical limitations (shadows less than 3 mm in size are not visible, quality of roentgen apparatus, sensitivity of film and the like), physical constitution of the patient is important, and so is sex (the breasts in women make analysis of the basal parts of lungs more difficult). All this has negative influence on the sensitivity of this radiologic examination, hence a significant percentage of false negative findings. Kipen et al.27 found normal lung findings on chest x-rays of 10%-20% of patients with pathohistologically confirmed asbestosis. Mathieson et al. report on similar results in a series of 118 patients with chronic diffuse interstitial pulmonary diseases, where plain x-ray diagnosis was accurate in 77% of patients, whereas chest CT results were accurate in as many as 93% of patients²⁸.

The results of our study (Table 1) almost fully correspond with the results obtained by Aberle *et al.*²⁹, both for the group of patients with chest x-ray findings (ILO categories 0/0 and 0/1), and for a larger group of patients with pathologic findings on chest CT x-ray films (ILO categories 1/0, 1/1 and $\geq 1/1^{1}$. Similar results have also been reported by Naidich³⁰, while Valeyre and Letourneux³¹ consider HRCT the most important examination in diagnosing minimal changes or mild pulmonary asbestosis.

The degree of agreement between the observers interpreting pulmonary/pleural pathologies from the same chest films by using ILO classification differs for different studies. The results of our study (Fig. 3) show higher agreement of observers in coding lung changes than the study of Impivaar *et al.*³², while the results on pleural changes are almost identical. The highest agreement among different observers in our series was recorded for ILO categories 0/0 and 0/1 (Fig. 4). According to Kappa test, the agreement result for these categories of profusion was "good", while in reality it was almost "excellent". For ILO categories 1/0, 1/1 and $\approx 1/1$ (clearly defined pulmonary asbestosis finding), the observer agreement was lower, and according to Kappa test it was "good".

Conclusion

Benign pulmonary/pleural asbestosis is a consequence of a longer period of inhalation of asbestos particles/fibers. Pulmonary asbestosis in the form of non-specific interstitial lung fibrosis of different stages is dominant in cases of chrysotile inhalation, and pleural asbestosis in the form of plaques and/or diffuse pleural thickenings is more often caused by inhalation of crocidolite.

Our study has revealed that reading of plain chest films as per ILO criteria is not sufficient for making or excluding the diagnosis of pulmonary/pleural asbestosis. This particularly holds for the initial stage of the disease, when a significant percentage of chest roentgenogram findings are within the normal limits (ILO categories 0/0 and 0/ 1). In such cases, when exposure to asbestos is confirmed and after a longer latency period, it is imperative to perform chest HRCT. If possible, the scanning should be performed on approximately 10 levels with a 2-cm distance between slices, slice thickness 1 mm and scanning time \leq 1 s. For its high sensitivity and accessibility, this method should become a routine algorithm of diagnostic procedures for different forms of asbestosis.

References

- International Labour Organisation, ILO. International classification of radiographs of pneumoconioses. Occupational Safety and Health Series XX. Geneve: ILO, 1980.
- KRAUS T, RAITHEL HJ, HERING KG. Evaluation and classification of high-resolution computed tomographic findings in patients with pneumoconiosis. Int Arch Occup Environ Health 1996;68:249-54.
- JANKOVIĆ S, ŠIMUNDIĆ I, TOCILJ J, MIŠE K, PERIĆ I, ROJE M, GJURKOVIĆ U, ČAPKUN V. Radiološke metode u dijagnostici bolesti uzrokovanih azbestom. Rad sigur 2001;5:13-26.
- FARZAN S, FARZAN D. Diagnostic methods, functional assessment and monitoring. In: Farzan S, Farzan O, eds. Respiratory diseases. 4th ed. Stamford, Connecticut: Appleton and Lange 1997;25-62.
- GENEREUX GP. Pattern recognition in diffuse lung disease. Med Radiogr Photogr 1985;61:2-31.
- GRENIER F, VALEYRE D, CLUZEL P, BRAUNER MW, LENOIR S, CHASTANG C. Chronic diffuse interstitial lung disease: diagnostic value of chest radiography and high-resolution CT. Radiology 1991;179:123-32.

- 7. Determination of airborne fibre number concentrations a recommended method, by phase contrast optical microscopy (membrane filter method), Geneva: World Health Organisation, 1997.
- KAMMP DW, WEITZMAN SA. Asbestosis. Clinical spectrum and pathological mechanisms. Proc Soc Exp Biol Med 1997;214:12-26.
- STEPHENS M, GIBBS AR, POOLEY FD, WAGNER JC. Asbestos-induced pleural fibrosis: pathology and mineralogy. Thorax 1987;42:583-8.
- CULLEN MR, CHERNIACK MG, ROSENSROCK L. Occupational medicine. Medical progress. N Engl J Med 1990;322:259-311.
- GLOAG D. Asbestos fibres and environment. BMJ 1981;282:623-6.
- MURAI Y, KITAGAWA M. Asbestos fibre analysis in nine lung cancer cases with high asbestos exposure. Arch Environ Health 1995;50:320-7.
- BONN D. Asbestos the legacy lives on. Lancet 1999;353:1336-9.
- 14. MURAI Y, KITAGAWA M. Asbestos body formation in the human lung: distinctions, by type and size. Arch Environ Health 1995;50:9-25.
- MCDONALD JC, ARMSTRONG B, DOELL D, MCCAUG-HEY WT, MCDONALD AD, SEBASTIEN P. Mesothelioma and asbestos fibre type: evidence from lung tissue analyses. Cancer 1989;63:1544-7.
- TIMBRELL V. The inhalation of fibres. In: Shapiro HA, ed. Pneumonoconiosis. Proceedings of the International Conference, Johannesburg, Cape Town' Oxford University Press, 1970:3.
- WAGNER JC, BERRY G, SKIDMORE JW, TIMBRELL V. The effects of inhalation of asbestos in rats. Br J Cancer 1974;29: 252-69.
- DAVIS JMG, BECKETT ST, BOLTON RE, COLLINGS P, MIDDLETON AP. Mass and number of fibres in the pathogenesis of asbestos-related disease in rats. Br J Cancer 1978;37:673-87.
- TIMBRELL V, POOLEY F, WAGNER JC. Characteristics of respirable asbestos fibres. In: Shapiro HA, ed. Pneumonoconiosis. Proceedings of the International Conference, Johannesburg, Cape Town, Oxford University Press, 1970:120.

- LANDRIGAN PJ, NICHOLSON WJ, SUZUKI Y, LADOU J. The hazards of chrysotile asbestos: a critical review. Ind Health 1999;37:271-80.
- BLAŽIĆ R. Profesionalna azbestoza u brodogradilištu "Uljanik". Zbornik radova, Simpozij o azbestozi i drugim azbestom izazvanim bolestima, Split, 27.-29. 9. 2001:12-4.
- PORETTI D. Osvrt na dvadesetogodišnje radiološko iskustvo u proučavanju azbestoze. Simpozij o azbestozi i drugim azbestom izazvanim bolestima, Split, 27.-29. 9. 2001:49-51.
- MURAI Y, KITAGAWA M. Fibre analysis in lungs of residents of a Japanese town with endemic pleural plaques. Arch Environ Health 1995;52:263-9.
- STANTON MF, LAYARD M, TEGERIS A, *et al.* Relation of particle dimension to carcinogenicity in amphibole asbestos and other fibrous minerals. J Natl Cancer Inst 1981;67:965-75.
- 25. NAYEBZADEH A, DUFRESNE A, CASE B, *at al.* Lung mineral fibres of former miners and millers from Thetford-Mines and asbestos regions: a comparative study of fibre concentration and dimension. Arch Environ Health 2001;56:65-77.
- 26. HILLERDAL G. Pleural lesions and ILO classification: the need for a revision. Am J Ind Med 1991;19:125-30.
- KIPEN HM, LILIS R, SUZUKI J, VALCIUKAS JA, SELI-KOFF IJ. Pulmonary fibrosis in asbestos insulation workers with lung cancer: a radiological and histopathological evaluation. Br J Ind Med 1987;44:96-100.
- MATHIESON JR, MAYO JR, STAPLES CA, MULLER NL. Chronic diffuse infiltrative lung disease: comparison of diagnostic accuracy of CT and chest radiography. Radiology 1989;171:111-6.
- Aberle DR, Gamsu G, Ray CS, Fenerstein IM. Asbestos-related pleural and parenchymal fibrosis: detection with high-resolution CT. Radiology 1988;166:729-34.
- NAIDICH DP. PULMONARY PAREnchymal high-resolution CT: to be or not to be. Radiology 1989;171:22-4.
- VALEYRE D, LETOURNEUX M. Asbestosis. Rev Mal Respir 1999;16:1294-307.
- 32. IMPIVAARA O, ZITTING AJ, KUNSELA T, ALANEN E, KERJALAINEN A. Observer variation in classifying chest radiographs for small lung opacities and pleural abnormalities in a population sample. Am J Ind Med 1998;34:261-5.

Sažetak

KLINIČKO-RADIOLOŠKE MANIFESTACIJE AZBESTNE BOLESTI OVISNO O MINERALOŠKIM SVOJSTVIMA AZBESTA

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Prikazana je zastupljenost plućne, odnosno pleuralne azbestoze ovisno o mineraloškim svojstvima azbesta, kao i osjetljivost rentgenograma prsiju i visokorezolucijske kompjutorizirane tomografije prsiju u analizi ovih promjena. Retrospektivnoprospektivna studija obuhvatila je 109 ispitanika - radnika tvornice azbestnih proizvoda Plobest d.d. iz Ploča (1. skupina, inhalacija pretežito azbesta krizotila) te 216 zaposlenika tvornice Salonit d.o.o. iz Vranjica kod Splita i Brodograđevne industrije Split (2. skupina, inhalacija pretežito azbesta krocidolita), u kojih je utvrđena azbestoza pluća i/ili plućnih maramica. Statistička obrada podataka učinjena je Kappa testom, c2-testom i analizom varijance, a rezultati ispitivanja prikazani su u grafikonima i tablici. Azbestoza pluća je utvrđena u 38 (35%), azbestoza pluća i pleure u 49 (45%), a azbestoza pleure u 22 (20%) ispitanika 1. skupine (izloženi krizotilu). U 2. skupini ispitanika (veća zastupljenost izloženosti krocidolitnom azbestu) azbestoza pluća je utvrđena samo u 9 (4%) ispitanika, azbestoza pleure u 117 (54%), a azbestoza pleure i pluća u 90 (42%) ispitanika. U 1. skupini ispitanika u njih 35 (32,1% ukupnog broja ispitanika 1. skupine) s urednim nalazom rentgenograma prsiju (International Labour Organisation /ILO/ kategorije prožetosti 0/0 i 0/1) visokorezolucijska kompjutorizirana tomografija je otkrila početni ili umjereni stupanj intersticijske plućne fibroze. U interpretaciji rentgenograma prsiju utvrđena je dobra, gotovo odlična podudarnost trojice ispitivača za kategorije ILO prožetosti 0/0, 0/1 i 1/0, te dobra podudarnost za kategorije prožetosti ≥1/1. Za azbestozu plućnih maramica u 1. skupini utvrđena je odlična podudarnost dvojice ispitivača (Kappa test = 79%), a u 2. skupini dobra podudarnost. Azbestoza pluća je znatno žešća u osoba izloženih inhalaciji krizotila, a azbestoza plućnih maramica u onih izloženih inhalaciji krocidolita. U radiološkoj dijagnostici, uz ILO klasifikaciju, preporučuje se u algoritam pretraga obvezatno uvesti visokorezolucijsku kompjutoriziranu tomografiju, poglavito u početnim stadijima bolesti pluća i pleure.