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Chest CT screening of asbestos-exposed workers: lung lesions and incidental findings

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Abstract

The objective of this study was to determine the feasibility of chest computed tomography (CT) in screening for lung cancer among asbestos-exposed workers.

All 633 workers included in the study were examined with chest radiography and high-resolution computed tomography (HRCT). Current and ex-smokers (cessation within the past 10 years) were also screened with spiral CT (N=180). Noncalcified lung nodules were considered positive findings. The incidental CT findings not related to asbestos-exposure were registered and further examined if needed.

Noncalcified lung nodules were detected in 86 workers. Five histologically confirmed lung cancers were found. Only one of the five cancers was detected also by plain chest radiography and three were in the group with a pre-estimated lower cancer probability. Two lung cancers were stage Ia and were radically operated. Altogether 277 persons had 343 incidental findings of which 46 required further examination. Four of these were regarded as clinically important.

CT and even HRCT proved to be superior to plain radiography in detecting lung cancer in asbestos-exposed workers with many confounding chest findings. The numerous incidental findings are a major concern for future screenings, which should be considered for asbestos-exposed ex-smokers and current smokers.

Keywords: asbestos, computed tomography, incidental findings, lung cancer, occupational exposure.

Introduction

Asbestos exposure induces a variety of benign and malignant pleural and lung diseases. Lung cancer is the most common asbestos-induced neoplasm. Its risk is associated with the intensity and duration of the exposure and the occurrence of asbestosis [1-3]. Cigarette smoking and exposure to asbestos interact in a strong synergistic fashion [4, 5]. The prognosis of lung cancer is poor: the 5-year survival rate is 10% in Finland, and it has not improved over time [6]. One of the reasons for the poor prognosis is the late diagnosis, when the tumor is already locally disseminated or metastatic. At an early stage, when the cancer is surgically resectable, the 5-year survival rate ranges from 55% to 72% [7] and even 76% survivorship have been reported [8].

The development of computed tomography (CT) has improved the sensitivity and specificity of imaging. Asbestos-related parenchymal and pleural changes can be detected with high-resolution computed tomography (HRCT) more sensitively than with plain chest radiography [9, 10]. Spiral CT is capable of finding small lung nodules and thus also lung cancer in an earlier and more curable stage [11-13] and it can detect more such nodules than plain radiography [11, 12]. CT has proved to be sensitive also when used to examine asbestos-exposed workers with confusing lung and pleural pathology [14]. It also detects other diseases in the examined area [13, 15].

The objective of this project was to employ HRCT as the imaging method for pulmonary and pleural diseases possibly present in Finnish workers exposed to asbestos and to assess the feasibility of lung cancer screening with spiral CT among the exposed smokers. This part of the study focuses on lung nodules and malignant lung tumors. Incidental findings are also considered in detail.

Study population and methods

Study design

The study was a cross-sectional baseline screening study for lung cancer among asbestos-exposed workers. In addition to benign and malignant lung lesions incidental findings were noted and their relevance evaluated. This study was carried out in 2003 and 2004. The asbestos-exposed workers were imaged with HRCT to find occupational lung and pleural diseases. Those who were current or ex-smokers (cessation within the last 10 years, N=180), were also screened with unenhanced low-dose spiral CT to detect lung cancer. Spiral CT was scheduled for this group because it was estimated that it has a higher risk of lung cancer due to the cumulative effect of asbestos-exposure and cigarette smoking. To avoid the unnecessary radiation exposure, the estimated lower-risk group was not screened with spiral CT. Smokers older than 70 years and those presumed not to be operable were excluded from the spiral imaging [16].

Study population

The study population consisted of three groups (A, B, C). Workers in group A participated in the asbestos screening program of the Finnish Institute of Occupational Health (FIOH) in 1990-1992 due to their occupational exposure and had no diagnosed asbestos disease at that time [17, 18]. From all those screened, we selected persons who were heavily exposed (exposure index more than 70) [1] and who lived in three geographic areas (Helsinki, Tampere and Turku and their surroundings). Workers with asbestosis (group B) and workers with asbestos-related pleural findings (group C) who visited clinics of occupational medicine in Helsinki and Tampere for a clinical follow-up and were willing to participate in the study formed the remaining two groups.

All of the participants gave their written informed consent, and the study protocol was accepted by the local ethical committee.

Methods

Posterioanterior chest radiographs were taken in each center (Helsinki, Tampere, Turku). CT of the chest was performed with three different scanners, two single slice scanners (Siemens Somatom Balance in Helsinki and a Siemens Somatom Plus 4 in Tampere) and one multislice scanner, a GE Lightspeed 16 Advantage (Turku). HRCT images were obtained during a full inspiration in a prone position. The slice thickness was 1-1.25 mm, and slices were taken at 3-cm intervals from the lung apex to the costophrenic angle. The imaging parameters were 130-140 kV and 100-111 mA. The images were reconstructed with the use of a high spatial reconstruction algorithm and were printed as hard copies at window settings (depending on the center) appropriate for viewing the lung parenchyma and soft tissues. Spiral CT images were exposed in supine position and at full inspiration. The slice thickness was 10 mm with a 15-20 mm table feed (110-120 kV, 36-110 mA). The images were reconstructed as 10-mm slices.

The chest radiographs were interpreted by a single reader (TVe in Helsinki, RJ in Tampere) separately from the CT image analysis as a routine clinical procedure. Attention was paid to possible lung shadows suggestive of a tumor. The (HR)CT images were analyzed, and findings were recorded by two radiologists in consensus (TVe and TA read the Helsinki images, and RJ and

TVi read the Tampere and Turku images). The readers were aware that the participants had been exposed to asbestos, but were blinded as to their medical data.

The presence, number, and size of the lung nodules were recorded. If there was a benign-type calcification or fat in the nodule and the nodule was <20 mm in diameter, it was considered benign [11, 19]. A finding suspicious of lung cancer was a lung nodule, that did not match these criteria and that had appeared or increased in size since the previous examination. A suspicious lesion was immediately re-examined with the use of thinner slices (3mm).

Noncalcified lung nodules were examined further according a modification of the protocol used in the Early Lung Cancer Action Project (ELCAP) study [11]. If the nodule was $\leq$5 mm in diameter it was re-examined with spiral CT after 6 months and again after 12 months. The growth of these nodules was noted accordingly to both visual assessment and measurement on screen. The slice thicknesses and imaging parameters were individually selected in these cases. For nodules 6-10 mm in diameter, the protocol recommended a biopsy thoracoscopically or with CT guidance. Alternatively, the nodule was re-examined after 3 months and, if needed, then similarly treated as previously described. When nodules were $\geq$11mm in diameter, a biopsy was recommended. All previous chest radiographs and CT images were reviewed when available.

All incidental CT findings were also registered. The radiologist informed the clinicians, who decided whether additional examinations were needed or not. Expert meetings were also used to solve problematic cases.

Results

A total of 633 (83.5%) of the invited 758 workers attended the imaging study [627 men, 6 women, mean age 64.5 (range 45.3 – 86.9) years]. Altogether 372 were studied in Helsinki, 182 in Tampere, and 79 in Turku.

Of the study group, 566 (89.8%) were construction workers, of which 264 (41.8%) were plumbers, the rest being industrial, real estate and cleaning workers. The mean duration of asbestos-exposure was 19.2 (range 0.5-45.5) years. There were 124 (19.9%) current smokers, 361 (58.0%) ex-smokers, 137 (22.0 %) never smokers, and 11 cases with lacking data of smoking. The mean number of smoked pack-years was 17.2 and the median was 18.8 (range 0 –129) pack-years for the whole group.

Noncalcified lung nodules were found in the CT (HRCT or spiral CT) scans of 86 [14%; 95% binomial confidence interval (CI) 11-17%] of the participants (n=633). Nodules were found in 45 of the CT/HRCT group and in 41 of the HRCT only group (CT/HRCT group: both HRCT and spiral CT were done, HRCT only group: only HRCT was undertaken). Of these 86 persons 56 had a single pulmonary nodule, 18 had two nodules, and 12 had three or more nodules.

According to the imaging protocol, 61 persons with nodules were followed with CT. Within 1 year, 38 of them had one follow-up CT scan, 16 had two CT scans and 7 had three. For 17 persons, nodules of similar size and location were also apparent in old CT scans, thus those seen in the current scans were evidently benign and needed no additional attention. Thirty-seven persons were admitted directly to the hospital for examination because of lung nodules (Fig 1). The final decision on how to proceed with the nodules was individually decided by the referring physician. There were three CT-guided transthoracic fine needle aspirations for lung nodules and one biopsy of a pleural lesion guided by ultrasound. Two mediastinoscopies and 12 bronchoscopies were performed as further investigations. Some of the repeated CT examinations were performed after hospital admission when other diagnostic examinations were unfeasible.

Five lung cancers were confirmed histologically (0.8%; Poisson CI 1.62-11.67) (Table 1). There was also one highly suspicious case for lung cancer, but because of poor lung function the patient was inoperable, and biopsy was not possible either due to thick pleural plaques between the lesion and the intended puncture site. The histologically confirmed cancers included two adenocarcinomas, two squamous cell cancers, and one poorly differentiated lung carcinoma. Two were stage Ia, and three were stage IIIb. One patient was initially felt to have a stage Ia cancer but at time of surgery, it was discovered that it was in fact stage IIIb. Three out of five cancers were found in the group scheduled for HRCT only, and one of them was a curatively operative stage Ia tumor. The chest radiography found only one cancer. All the lung cancers were found in patients who were current or ex-smokers, and in the contrary no lung cancers were found in non-smokers.

In addition, one pleural mesothelioma was found, and it was regarded as an occupational disease, bringing the total number of verified malignancies to six (1,0%; Poisson CI 2.20-13.06). This patient received chemotherapy. There were four thoracotomies performed, that revealed no malignancy. Two benign lung nodules were operated on: One was a 1.7-cm tuberculotic nodule, and other was a hamartoma. Two patients with suspicious pleural nodules and effusions underwent thoracotomy, but the histopathological diagnosis was fibrosis.

No incidental malignancies were found. Among the 633 screened persons, 343 incidental lesions were detected in 277 (44 %; 95% Binomial CI 40-48 %). Most of these were coronary calcifications, cysts, or benign parenchymal scars or calcifications. Only the most evident coronary calcifications were recorded. Altogether 46 of the 343 lesions (13 %; 10- 17 %) in 42 persons were examined further and 33 of the persons were submitted directly to hospital (Fig 2). Some of the incidental findings were examined further with imaging methods (ultrasound, CT, magnetic resonance imaging), while some needed more invasive examinations (mediastino-, broncho-, thoracoscopy, biopsies). Seventeen thoracic findings (pleural effusions, mediastinal lymph nodes, tracheal nodule, etc) required further examination, and they all proved to be benign. Four of the further evaluated 29 abdominal findings were considered clinically significant (an adenoma producing aldosteron, trombocytopenia detected in a person with splenomegalia, cirrhosis of the liver causing ascites, and ascites because of heart failure). Most of the findings that led to additional examinations proved to be benign lesions like cysts or adrenal incidentalomas. One liver biopsy was made for multiple hemangiomas.

Discussion

Spiral CT and even HRCT detected more lung nodules and lung cancer in asbestos-exposed workers than chest radiography [11, 12]. Numerous incidental findings not associated to the occupational exposure were also noted. We imaged 633 asbestos-exposed persons with HRCT, and 180 of them also with spiral CT. Noncalcified lung nodules were found in 86 (14%) persons. Five verified lung cancers were found. Two of the lung cancers were in stage Ia and were curatively operated on. We found 343 incidental findings, and 46 of them needed additional examination. Four of these were judged to be clinically important.

Periodical health examinations of asbestos-exposed workers are mandatory in Finland [18]. The participants in our study were asbestosis patients and asbestos-exposed workers with or without pleural plaques. Pleural plaques and calcifications make the analysis of the lung parenchyma difficult with the use of conventional chest radiography. Spiral CT has proved to be valuable in detecting focal masses that may be obscured by pleural or parenchymal fibrosis [20], as in four of our cancer patients. In our study, HRCT detected lesions in 41 workers, who were primarily not imaged with spiral CT, of which three were lung cancers and one was a mesothelioma. Remy-Jardin et al examined asbestos-exposed workers with HRCT and spiral CT in the same session [21]. They reported that spiral CT depicted lung nodules in 17 persons that were missed in HRCT examinations. Asbestos associated lung parenchymal diseases are increasingly imaged with HRCT, but, when the target of screening is primarily lung cancer, HRCT should not replace spiral CT.

We found noncalcified nodules in 14% of the participants. In previous studies, noncalcified lung nodules have been found in 18.4 – 51 % of the study population [11, 13, 14, 15, 22]. The range of the number of lung nodules found is wide and may partly be due to the different prevalences of granulomatous infections [13]. Also the variability in imaging techniques may explain the difference while the studies that used a smaller collimation of 5 mm or less, reported the highest rate of noncalcified nodules [13, 22]. We found fewer noncalcified nodules than others and probably the major reason for this was that not all of our participants were studied with spiral CT.

We found lung cancer in 0.8% of the participants. The lung cancer detection rate differs considerably between the referred studies; 0.46-2.7% [11, 13, 14, 15, 22]. This may be due to differences in the smoking habits, age, and possibly occupational exposure of the populations. The median pack-years in four studies [11, 13, 15, 22] was 45 in each of them, while the smoking history in our study was lower (median 18.8 pack-years). It was surprising that, inspite of both asbestos-exposure and smoking among our participants we did not find more cancers. Our cancer detection rate was, however, quite comparable with most of the articles. It seems that the low risk due to limited tobacco smoking was compensated with an increased risk from asbestos exposure. It is also possible that false negatives cancers occurred due to gaps between slices while screening of the "HRCT only" group.

In the year 2000 an international specialist group presented recommendations for the CT screening of asbestos-exposed workers [23]. It concluded that spiral CT has great potential in the screening for lung cancer of well defined high-risk groups. No practical recommendation was given for such screening, but they suggested systematic screening projects. We tried to study the value of both spiral CT and HRCT in lung cancer screening of asbestos-exposed workers, while there are no previous studies concerning the matter. We included only the high risk workers in the spiral CT group due to radiation exposure reasons. The groups turned out not to be optimal because there were more cancers in the lower risk group. The smoking history criteria (current active smoker or ex-smoker with the cessation within the last 10 years) used as part of our current protocol may have been too strict for current or former workers with asbestos exposure.

There were no statistical differences between the five cancer patients and the rest of the screened persons with respect to the mean age, asbestos exposure index or smoking habits (one-way analysis of variance) (Table 2). The only difference between the groups was that all of the participants with a detected lung malignancy had smoked, and no lung cancers were detected among non-smokers. To determine the benefit of CT in lung cancer screening needs further randomized controlled trials with an adequate follow-up of all participants. Such trials are now underway [24, 25], and the results may give us more information of the feasibility of the screening. If screening for lung cancer is effective, then those current and ex-smokers who are asbestos exposed should be included in the screening group.

Lung cancer screening with low-dose CT has been shown to detect numerous indeterminate lung nodules [11-15, 22], of which the vast majority are benign and therefore make cancer detection difficult. The diagnostic work-up should find small lung cancers as early as possible and unnecessary surgery of benign nodules should be avoided. However, no standard approach for the diagnostic work-up currently exists. In most screening studies, the assessment of growth rate has been the main technique applied [11, 12, 14, 15, 22]. Henschke reported that, in ELCAP studies, 94% of the recommended biopsies resulted in a diagnosis of malignancy and no lobectomies were performed for benign disease [26]. In other lung cancer screening studies this kind of result has been difficult to achieve [13, 15, 22]. In our study three lung biopsies for nodules were done, and none of them proved to be malignant, while two benign nodules were operated on.

We detected incidental findings in 44% of the participants. Additional examinations were needed for 7.3% of those screened and clinically important findings were regarded to exist for 0.6%. MacRedmond et al reported incidental findings in 61.5%, and significant findings in 49.2% of their lung cancer screening population [15], while Swensen et al detected significant findings in 14% and incidental malignancy in 7.9% [13]. We did not find any incidental malignancies. The definition of the incidental findings and their significance varied (Table 3). Such findings may save additional lives, but they can also lead to a series of unnecessary examinations, as in our study, in which most of such findings proved to be benign. On the other hand, the value of some incidental findings such as coronary calcifications, as risk factors is not yet fully known.

After screening examinations many participants need follow-up CT scans or other examinations for noncalcified lung nodules or incidental findings. This necessity not only adds to the cost of the screening, but may also increase anxiety and feelings of sickness among participants [27, 28]. These psychological factors seem to have gained little attention in the literature.

In lung cancer screening, attention should also be paid to the radiation dose. With spiral CT, we used similar or a slightly higher mA value (36 - 110) than the latest screening programs (40-50 mA) [10-12]. In low-dose CT the effective dose range is 0.3-0.65 mSv [13, 29] while with conventional CT the range is 3-27 mSv [29]. A screen-detected lung nodule may lead to one or more additional diagnostic CT examinations and thus increase the dose. According to Brenner [30] a mortality benefit of more than 5% would be needed to outweigh the potential radiation risks of annual CT screening.

Conclusion

In conclusion spiral CT screening, and in some cases even HRCT, seems to be sensitive in revealing malignant tumors in asbestos-exposed persons despite their abundant pleural and pulmonary pathology. The problems of screening include the optimal selection of the target group, the large number of benign lesions both in the lungs and elsewhere and iatrogenic hazards such as radiation exposure and unnecessary investigations caused by irrelevant findings. Screening for lung cancer among this asbestos exposed group yielded roughly a similar amount of cancers than previous baseline screening trials, in which the participants had no significant asbestos exposure but usually a hevier smoking history.

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Figure 1: Nodules requiring additional examinations.
(CT= computed tomography, HRCT= high-resolution computed tomography, FIOH= Finnish Institute of Occupational Health, FNA= fine-needle aspiration, diff= differentiated)

Figure 1.

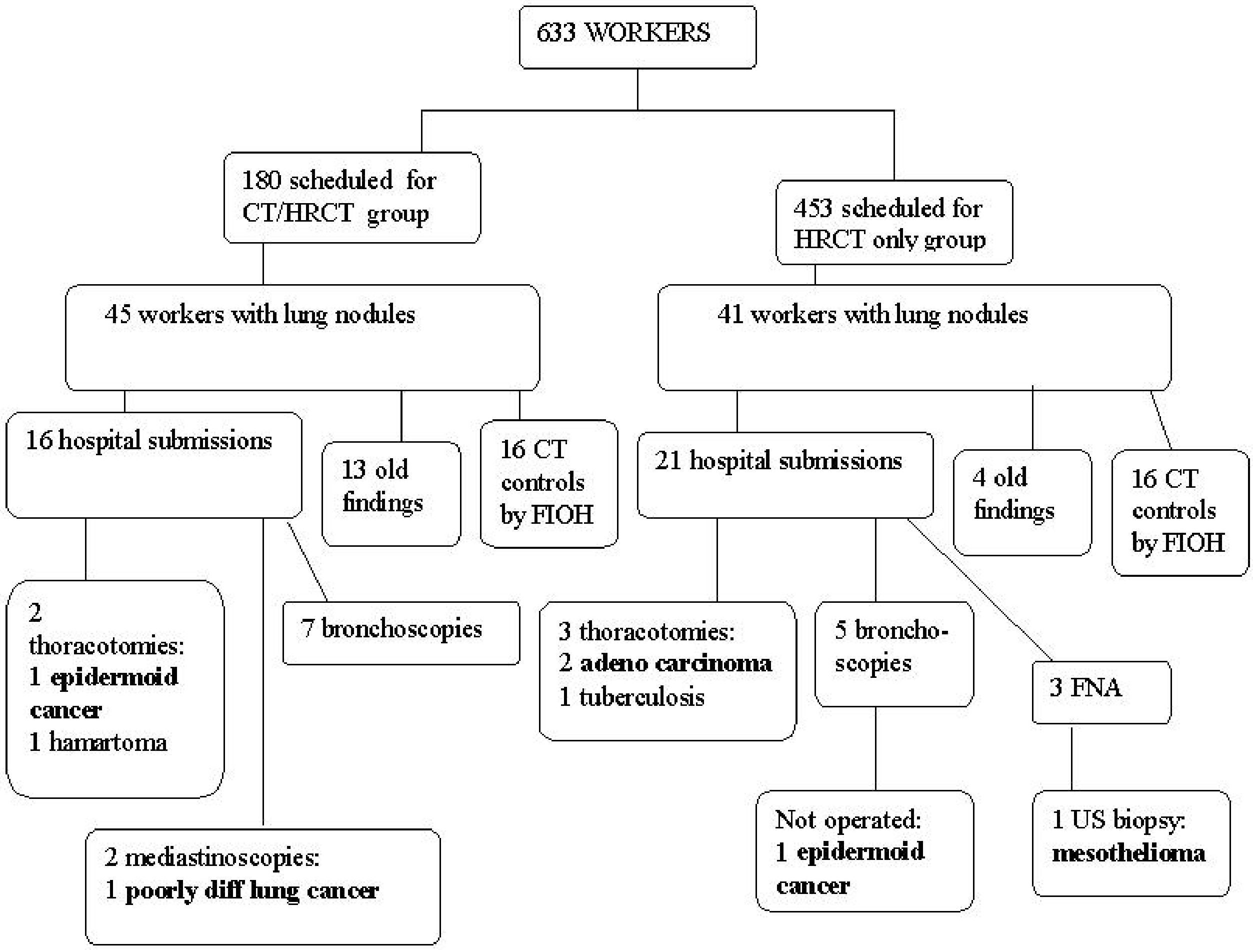

Figure 2: Incidental findings requiring additional examinations.
(CT= computed tomography, HRCT= high-resolution computed tomography, US= ultrasound, FIOH= Finnish Institute of Occupational Health, MRI= magnetic resonance imaging, FNA= fine-needle aspiration)

Figure 2.

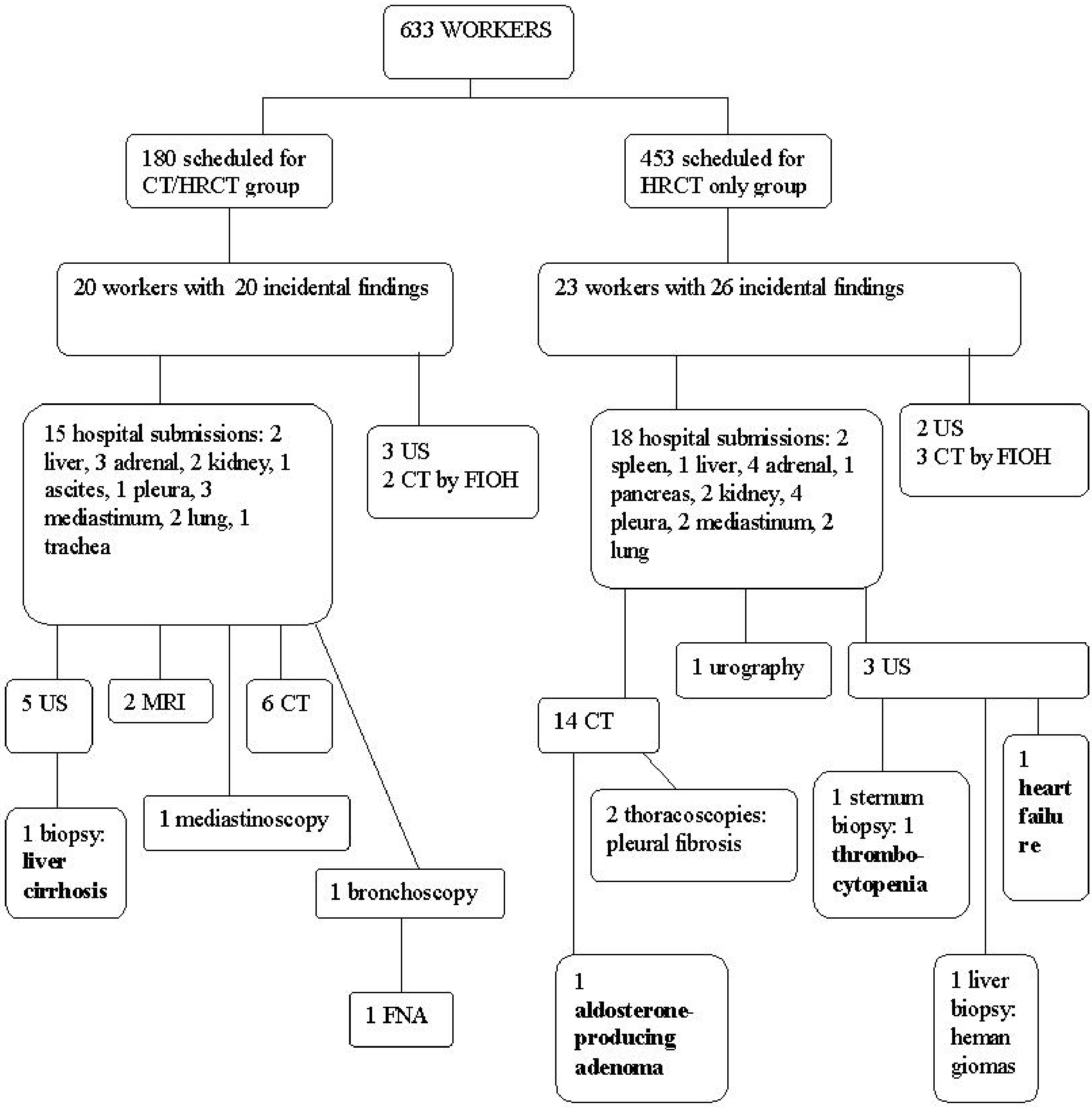
633 WORKERS
180 scheduled for CT/HRCT group
453 scheduled for HRCT only group
20 workers with 20 incidental findings
23 workers with 26 incidental findings
15 hospital submissions: 2 liver, 3 adrenal, 2 kidney, 1 ascites, 1 pleura, 3 mediastinum, 2 lung, 1 trachea
3 US
2 CT by FIOH
18 hospital submissions: 2 spleen, 1 liver, 4 adrenal, 1 pancreas, 2 kidney, 4 pleura, 2 mediastinum, 2 lung
2 US
3 CT by FIOH
5 US
2 MRI
6 CT
1 urography
3 US
14 CT
1 biopsy: **liver cirrhosis**
1 mediastinoscopy
1 bronchoscopy
1 FNA
2 thoracoscopies: pleural fibrosis
1 sternum biopsy: 1 **thrombo-cytopenia**
1 **heart failu re**
1 **aldosterone-producing adenoma**
1 liver biopsy: heman giomas

Table 1: Characteristics of patients with lung cancer

Characteristics	Patient 1	Patient 2	Patient 3	Patient 4	Patient 5
Age, years	66.0	67.5	68.2	73.4	65.5
Asbestos-exposure index	104.8	43.5	47.0	73.4	24.5
Smoking status	Current smoker	Ex-smoker[a]	Ex-smoker[a]	Ex-smoker[a]	Current smoker
Smoking, pack-years	43.0	10.0	10.0	28.9	13.3
Scheduled spiral CT	Yes	No	No	No	Yes
Tumor visible in chest radiography	No	Yes	No	No	No
Histology	Squamous cell cancer	Adeno-carcinoma	Adeno-carcinoma	Squamous cell cancer	Poorly differentiated lung cancer
Tumor stage	Ia	IIIb	Ia	IIIb	IIIb
Therapy	Operation, curative	Operation, non-curative	Operation, curative	Chemo-therapy	Chemotherapy
Histology was obtained in	Operation	Operation	Operation	Bronchoscopy	Bronchoscopy and mediastinoscopy
Pleural plaques	Yes	Yes	Yes	Yes	Yes
Asbestosis	Yes	No	No	Yes	No

[a] smoking cessation more than 10 years earlier

Table 2: Asbestos-exposure index, mean age, and smoking pack-years for the five lung cancer patients versus the rest of the participants

	Lung cancer [a]	N	Mean	Range	SD
Asbestos-exposure index	0	609	79.6	9.0-268.0	46.3
	1	5	58.6	24.5-104.8	31.1
Age, years	0	627	64.5	45.3-86.9	6.81
	1	5	68.1	65.5-73.4	3.1
Pack-years	0	460	22.7	0.5-129.0	17.3
	1	5	21.0	10.0-43.0	14.6

[a] 0= no cancer

[a] 1= lung cancer

Asbestos-exposure index: cumulative exposure index for the work career until the screening visit, which is calculated summing up the asbestos working years weighted by the respective estimated exposure levels [1].

Table 3: Incidental findings reported in three studies screening for lung cancer

Finding	Swensen et al [a]	MacRedmond et al [b]	Vierikko et al [c]	Vierikko et al [d]
	N %	N %	N %	N %
Emphysema		130 (29%)		
Bronchiectasis	11 (0.7%)	44 (9.8%)		
Arterial calcification	1 (0.1%)	64 (14.3%)	138 (21.8%)	
Other lung pathology	2 (0.1%)	17 (3.8%)	33 (5%)	4 (0.6%)
Pleural effusion/plaque/nodule	4 (0.3%)	4 (0.9%)	6 (1%)	5 (0.8%)
Goiter/thyroid nodule		9 (2%)	4 (0.6%)	
Aortic aneurysm	51 (3.4%)	1 (0.2%)	1 (0.2%)	
Bronchial/tracheal pathology	9 (0.6%)		2 (0.3%)	2 (0.3%)
Pericardial effusion	9 (0.6%)			
Atrial myxoma	1 (0.1%)			
Breast finding	17 (1.1%)		2 (0.3%)	
Breast cancer	3 (0.2%)			
Mediastinal lymphadenopathy			6 (1%)	6 (1%)
Ascites			2 (0.3%)	2 (0.3%)
Renal cell cancer	4 (0.3%)			
Benign/indeterminate hepatobiliary/renal/spleen disease	57 (3.8%)	41 (9.1%)	97 (15.3%)	16 (2.5%)
Adrenal pathology	36 (2.4%) (1 pheochromocytoma)		13 (2%)	9 (1.4%)
Pancreas			1 (0.2%)	1 (0.2%)
Gastric/ esophageal pathology	2 (0.1%)	4 (0.9%)	17 (2.7%)	
Spine metastasis	1 (0.1%)			
Lymphoma	2 (0.1%)			
Active endometriosis		1 (0.2%)		
Soft tissue nodule/calcification			19 (3%)	1 (0.2%)
Diaphragm eventration			2 (0.3%)	
Total	210	315	343	46

[a] Significant findings for 1520 participants.
[b] All findings for 449 participants.
[c] All findings for 633 participants.
[d] Additional examined findings.

The number indicates the amount of the individual abnormalities and the percentage is the proportion of the total study population with an individual abnormal finding.