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Post-occupational health surveillance of asbestos workers

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Parole chiave
Lavoratori dell'amianto; sorveglianza sanitaria; screening del cancro polmonare

Summary

Background: *Italian law requires an extensive health surveillance of workers after cessation of their employment status in the case of occupational exposure to carcinogens, including asbestos. Nonetheless, Italian law does not specify the timeframe of these clinical checks, nor who has financial and organizational responsibility for this surveillance. A literature search confirmed a lack of consensus around the objectives and methods to follow up workers with past occupational exposure to asbestos.* **Objectives:** *To develop an updated evidence-based methodology for an appropriate health surveillance programme.* **Methods:** *We present an overview of the field experience developed by the Veneto Region from 2000 to 2011, and new studies that could contribute to establishing a national policy for the medical surveillance of workers with past asbestos exposure.* **Results:** *There were three specific topics: (1) definition of a reliable method to identify asbestos workers (through multiple sources and procedures that meet current confidentiality*

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regulations); (2) detection of asbestos fibres in biological media (to support the etiological diagnosis of asbestos-related diseases); (3) creation of a national protocol of health surveillance (through the assessment of policies developed by other Regions in this field, and recruiting from these regions a cohort of past-exposed workers: the epidemiological study should offer relevant suggestions for specific surveillance approaches, based on either estimated cumulative asbestos exposure or detection of x-ray patterns of pleural plaques and/or asbestosis). **Conclusions:** *These studies will support the Regions in setting up health care policies directed at workers with past asbestos exposure.*

Riassunto

«Sorveglianza sanitaria post-occupazionale dei lavoratori dell'amianto». **Introduzione:** *La legge italiana prevede la sorveglianza sanitaria dei lavoratori dopo la cessazione del lavoro nel caso di esposizione professionale a cancerogeni, tra cui l'amianto. Tuttavia, la legge italiana non specifica la periodicità della sorveglianza né a chi spetta la responsabilità finanziaria e organizzativa della stessa. Una ricerca della letteratura in materia ha confermato la mancanza di un protocollo condiviso di sorveglianza sanitaria dei lavoratori con pregressa esposizione professionale all'amianto.* **Obiettivi:** *Sviluppare una metodologia aggiornata basata sulle evidenze per definire un programma di sorveglianza sanitaria.* **Metodi:** *Viene presentata una panoramica delle esperienze sviluppate in questo campo dalla Regione Veneto dal 2000 al 2011, e nuovi studi che possono contribuire a progettare una politica nazionale per la sorveglianza sanitaria dei lavoratori dell'amianto.* **Risultati:** *I risultati sperati sono tre: (1) definizione di un metodo affidabile per identificare i lavoratori dell'amianto (attraverso l'utilizzo di più sorgenti e procedure che soddisfino le vigenti norme sulla privacy); (2) rilevazione delle fibre di amianto nei mezzi biologici (per consentire la diagnosi eziologica di malattie da amianto); (3) creazione di un protocollo nazionale di sorveglianza (attraverso la valutazione delle esperienze sviluppate da altre Regioni Italiane in materia e reclutando in queste regioni una coorte di lavoratori ex-esposti: lo studio epidemiologico dovrebbe offrire elementi di supporto per specifiche modalità di sorveglianza, basate sull'esposizione all'amianto o sulla presenza di segni radiologici di placche pleuriche e/o asbestosi).* **Conclusioni:** *Questi studi dovrebbero consentire alle varie Regioni Italiane la pianificazione di politiche di assistenza sanitaria dirette ai lavoratori dell'amianto.*

Background

Italian law requires an extensive health surveillance of workers after cessation of their employment status in the case of occupational exposure to carcinogens (Legislative Decree. 81/2008). Nonetheless, Italian law does not specify the timeframe of these clinical checks, nor who has financial and organizational responsibility for the surveillance.

According to the most recent regulations of the Italian National Health Service (NHS), the Italian Ministry of Health sets the main targets, while the Regions are responsible for appropriately planning and implementing local health policies to achieve such objectives.

A literature search confirmed a lack of consensus around which should be the objectives and methods to follow up workers with past occupational exposure to asbestos.

In this paper we present an overview of the work conducted in the Veneto Region in this field from 2000 to 2011, and the design of new studies that could contribute to setting up a national policy for the medical surveillance of workers with past asbestos exposure. In describing the health surveillance work already carried out, two major components (rather inter-connected in practice) were distinguished: clinical evaluation and exposure assessment.

Clinical evaluation

Active surveillance (2000 to 2005): the lung cancer screening project

In most industrialized countries, the incidence of lung cancer in asbestos workers is expected to peak between 2010 and 2020 despite regulatory

restrictions on asbestos use or bans imposed during the 1980s and 1990s (4). In the late 1990s, a study described an imaging method for early diagnosis of lung cancer (6). For these reasons, during 2000-2005, the Veneto Region developed a surveillance programme, co-founded by the Italian Ministry of Health, to assess the feasibility of low-dose computerized tomography (LDCT) as a screening test for early diagnosis of lung cancer. Categories of workers with the highest risk of asbestos exposure were selected: cement-asbestos workers, railway construction and repair workers, insulators, shipyards workers. Details of the screening programme had been previously published (9). Briefly, out of 2,000 employees contacted, 1,165 (58%=1,165/2,000) agreed to take part. The subjects were examined by the occupational physicians of the Health and Safety at Work Departments (SPSAL, Italian acronym) of 7 Regional Local Health Authorities (ASL, Italian acronym) using the same protocol to collect clinical and occupational history. The historical exposure to asbestos was retrospectively estimated using a questionnaire with job-specific modules (8) (see below). LDCT was performed using a follow-up protocol suggested by Henschke (6).

All patients were encouraged and supported to stop smoking. Out of the 1,165 patients examined, only five were cancer cases (4 primitive and 1 secondary). A further primitive case of lung cancer was diagnosed by cytology. Only one single early stage (IA) cancer case was observed, which is presumed to have a 70% survival chance after five years post-surgical removal. The estimated dose of ionizing radiations administered to 1,160 healthy subjects was around 1,100 mSv: about 1 mSv per each examined subject and 220 mSv for each screen-detected lung cancer case. The screening costs were estimated at about 1,066 Euros per subject examined and 248,000 Euros for each screen-detected lung cancer case. Lung cancer incidence was about 149 per 10^5 among 1,119 screened subjects (excluding women and workers with incomplete information), equal to males' in the regional population aged 55-59 years (the average age among screened workers was 57 years) according to the Veneto Tumour Registry in the same years. The programme was thus considered unsatisfactory because of low adherence, low number of cases detected, high cost and rather high radiation doses to healthy subjects (9).

Health surveillance on demand

As no advantage in terms of lung cancer prevention was achieved in the group with highest asbestos exposure, the screening programme was discontinued and, starting from 2006, the surveillance protocol was therefore changed. All workers, whatever the previous level of asbestos exposure, were offered health surveillance on demand, free of charge, focused on the diagnosis of non-malignant asbestos-related diseases (Decree No. 2041/2008 of the Regional Committee). The following surveillance protocol was designed:

- retrospective assessment of asbestos exposure using a questionnaire (see below);
- medical examination to diagnose chronic bronchitis/emphysema (because they were associated with a high risk of lung cancer in 17,698 heavy smokers previously exposed to asbestos (7));
- history of cigarette smoking (since combined exposure to asbestos and cigarette smoking showed a more than additive effect on risk of lung cancer (17));
- lung function test (because asbestos workers with FEV1/FVC ratio <60% showed a four-fold increase in lung cancer risk (3));
- conventional chest x-ray (followed by LDCT in presence of symptoms and/or clinical signs, as established by Legislative Decrees 230/95 and 187/2000);
- other examinations or specialist consultations if required;
- anti-smoking counselling;
- subsequent medical check after at least three years, on demand.

Table 1 shows the number of medical services delivered and the number of malignant and non-malignant asbestos-related diseases diagnosed.

Figure 1 shows an increasing temporal trend of clinical evaluations and chest x-rays performed, whereas LDCT were stable or decreasing.

Table 1 - Health care provided to past asbestos workers, Veneto Region, from 2006 to 2011 (and total): outpatient examinations; low-dose computed tomography (LDCT); chest x-ray (XR); and number of diagnoses of: pleural plaques (PP), asbestosis (A), lung cancer (LC), malignant mesothelioma (MM)

Year	Examinations	LDCT	XR	PP	A	LC	MM
2006	640	381	31	38	3	5	1
2007	915	465	89	57	6	5	4
2008	1071	383	111	79	12	4	1
2009	1230	506	132	70	5	3	4
2010	1276	385	145	35	10	2	2
2011	1137	360	161	73	2	7	2
Total	6269	2480	669	352	38	26	14

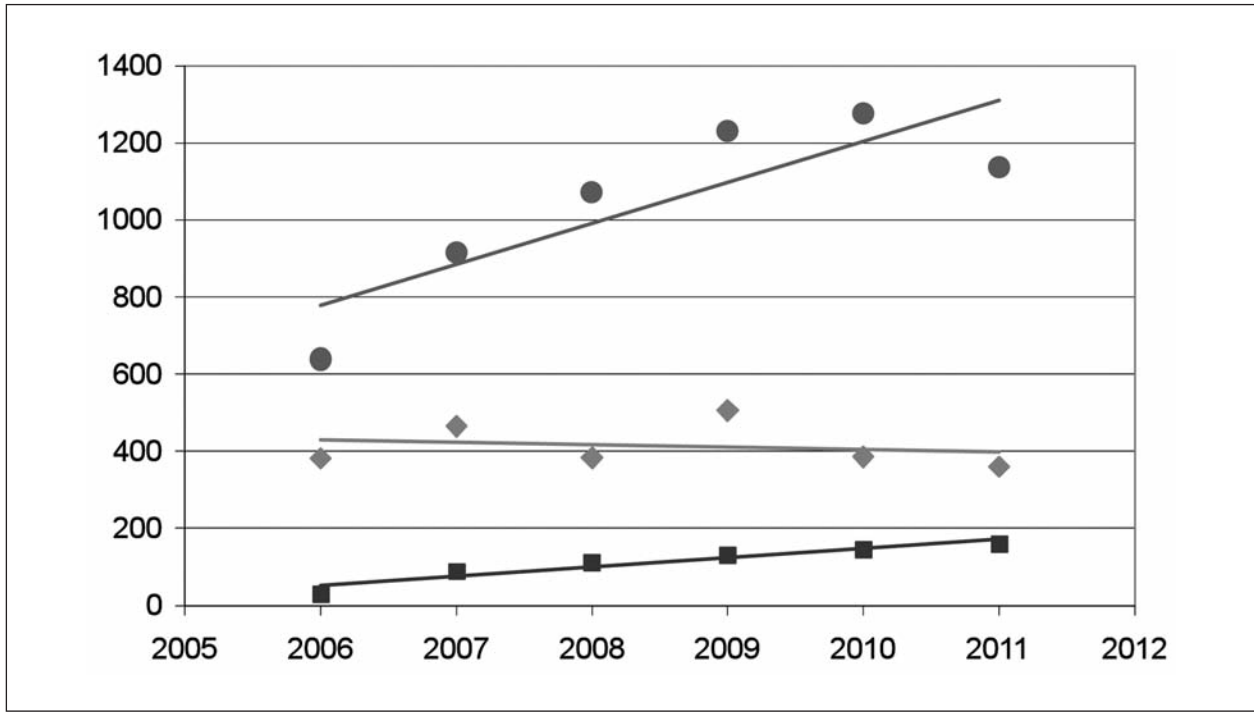

Figure 1 - Clinical examinations (●), LDCT (◆) and XR (■) by calendar year

Exposure assessment

Questionnaire

Historical exposure to asbestos was retrospectively estimated using a questionnaire with job-specific modules (8), to guide interviewers in the process of collecting the relevant information about the workplace, factory's work sector and exposure to mineral fibres. Estimation of occupational exposure was carried out by occupational physicians of SPSAL, according to a stepwise procedure:

- in the initial assessment the materials used, their content of asbestos fibres and their friability were evaluated. Then workers' duties were examined in terms of mechanical stress applied to the materials with the tools used. Lastly, local factors influencing exposure were

also evaluated, such as for instance the presence of local aspirators, the surface of the sources, the size and characteristics of the building, etc. For each of these different aspects of exposure, an ordinal assessment was provided based on scales codified by proper tables;
- the integration of different scores leads to the semi-quantitative estimation of the concentration (i) which, with the percentage of work time spent at that concentration (f) and the years of exposure time (d), allows an estimation of the cumulative asbestos exposure (= i×f×d). If a subject had changed duties or factory, the cumulative exposure was the sum (= Σ (i×f×d)) of as many products as those necessary to take into account the whole occupational history.

Out of 1,165 workers of the Veneto Region examined from 2000 to 2005, in 772, for whom asbestos exposure was estimated by questionnaire, significant risk factors for diseases diagnosed by LCDT were: cumulative exposure for asbestosis (trend=0.004); time elapsed since first exposure (p trend=0.001) and peak of exposure (p trend<0.001) for pleural plaques (PP); time since first exposure for diffused pleural thickening (p trend=0.024). These results were consistent with studies performed by traditional chest x-ray, and in some way confirmed a correct estimation of the historical exposure to asbestos (10).

Bio-markers: Osteopontine

Even if asbestos exposure assessed by questionnaire was precise and accurate, the estimation procedure was difficult, complicated, long, and could suffer from subjective assessment. Other limits of this approach are: the difficulty in assessing the relative importance of the various determinants; the possibly low concordance between different interviewers; the variability of information collected from different study subjects (one individual could describe the details of duties performed, whereas another could only vaguely remember the name of the job) (11). Lastly, interviews could last more than an hour, with frequent discomfort for interviewees, who were frequently elderly. Osteopontine (OPN) is a plasma protein with important chemo-tactical and pro-inflammatory activities, produced in excess in cancer of the lung, breast, colon-rectum, stomach, ovaries and melanoma. Pass (15) reported that OPN blood levels were correlated with the duration of occupational asbestos exposure and the presence of radiographic signs in a limited number of subjects. In order to confirm these results OPN plasma levels were measured in 254 workers with past asbestos exposure (53 with asbestos-related benign diseases) and were associated with different aspects of asbestos exposure and presence/absence of pleural plaques. The results of the latter study showed that OPN was not a reliable biomarker neither for asbestos exposure nor for PP occurrence (11).

Objectives

The general objective of the planned future activities is to develop an up-dated evidence-based methodology for a health surveillance programme. The plan should address three specific aims:

Aim 1. Defining a reliable method to identify asbestos workers.

Aim 2. Detection of asbestos fibres in biological media.

Aim 3. Setting up a national surveillance policy.

Methods and designs of future studies

Defining a reliable method to identify asbestos workers

Available sources of asbestos workers are not exhaustive because:
- the Italian National Institute for Social Insurance (INPS) list of subjects submitting a claim for compensation benefits does not include workers retired before 1992;
- the list of the Italian National Institute for Compensation of Work-Related Diseases and Accidents (INAIL) underestimates this number if employers who did not declare risky work activities;
- the list of factories (kept by SPSALs) and buildings (kept by the Environmental Protec-

tion Agency) containing asbestos is available only if an official application for asbestos removal is submitted;
- a list of factories is available whenever cases of mesothelioma occur and are investigated by the National Registry of Malignant Mesothelioma (ReNaM, Italian acronym). No corresponding information is available for lung cancer cases.

We will test the feasibility of data cross-check procedures, applicable under the current legislation, in some areas of the Italian Regions. The list of asbestos workers can be put together through information exchanges between public and/or private administrations, but transfer of sensitive data is hampered by Italian confidentiality legislation. In order to overcome these difficulties we will involve SPSALs in developing a locally applicable standard procedure authorized under current regulations. This will be tested as a best standard practice for an exhaustive identification of asbestos workers.

The above cohort could be targeted by primary prevention (counselling for smoking cessation) and secondary prevention (early diagnosis once consensus on appropriate protocols is reached), and will be submitted to record linkage with regional health records, hospital discharge forms, mortality records and cancer registries (if available).

Detection of asbestos fibres in biological media

Asbestos fibres have been reportedly found in urine of subjects with occupational exposure to asbestos or drinking water contaminated with this mineral (12). The mineralogical analysis of urine and other biological samples has already been used to map environmental exposure to asbestos fibres (1,5). Therefore the present project aims to study the validity of the mineralogical analysis of urine as an asbestos exposure indicator. In this respect 50 Veneto workers with asbestos-related diseases will be recruited. Each subject will sign an informed consent for the collection of 20 cc of urine. Identification, count and analysis of asbestos fibres will be performed by electronic microscopy according to a standardized procedure (1). The results will be compared to asbestos exposure retrospectively estimated by a questionnaire.

Asbestos lung burden will also be assessed in individual cases of lung cancer and asbestosis. Since this measurement has a high variability, in order to discriminate occupational exposure from environmental background exposure, we will examine lung tissues from a series of 200 consecutive autopsies of subjects (coming from several provinces of Veneto) with no occupational asbestos exposure. To be representative for mineral analysis, the samples should be 2 cm^3 blocks taken from 3 anatomic sites in the opposite lung (for tumour cases) or both lungs (in non-tumour cases), from the higher apex, lower apex, and basal segments of the lung (16). Mineral fibre analysis will be carried out with Scanning Electron Microscopy (SEM) on lung tissue digests retrieved from paraffin wax blocks. Cost analysis will be performed as well as comparison of results with questionnaire information (when available).

Setting up a national surveillance policy

To establish an evidence-based and operationally-defined national protocol for health surveillance of past asbestos workers, we will work in three fields:
- firstly, we will overview the experiences in health surveillance of past asbestos workers developed by 18 Italian Regions (Veneto, Emilia Romagna, Toscana, Calabria, Liguria, Abruzzo, Lombardia, Valle d'Aosta, Sardegna, Provincia Autonoma di Trento, Provincia Autonoma di Bolzano, Umbria, Puglia, Piemonte, Friuli Venezia Giulia, Sicilia, Campania, Basilicata), and in particular the methods of: (1) tracking historical exposure to asbestos using already available databases (if existing) or otherwise using a reliable method to recall it retrospectively; (2) ascertaining smoking habits and presence of chronic bronchitis/emphysema by history taking and clinical examinations; (3) assessing the criteria (respiratory signs and/or symptoms) requiring radiographic evaluation (chest x-ray or LDCT) in order to obtain potential diagnostic or therapeutic advantages;
- secondly, we will recruit a cohort of former asbestos workers in these regions (investigated by CT scan) that should offer elements to support

specific surveillance approaches, based on either estimated cumulative asbestos exposure or presence of x-ray patterns of PP and/or asbestosis. For example, preliminary results from a cohort recruited in the Veneto Region (about 1,700 asbestos workers with or without PP or asbestosis) showed the following standardized mortality ratios: 1.05 (95% confidence interval 0.48-1.99) in workers without PP, 1.05 (0.48-2.00) in workers with PP but not asbestosis, 4.62 (0.56-16.7) in workers with asbestosis; the few cases of mesothelioma were not analyzed. Few comparable studies are available, e.g., Pairon (14) studied 5,287 male asbestos workers from four French regions, for whom chest computerized tomography scan was available. In a 7-year period of follow-up 17 incident cases of pleural mesothelioma were found. Survival regression analysis was used to estimate the risk of pleural mesothelioma, adjusted for age and time-varying exposure variables. A statistically significant association was observed between mesothelioma and PP (adjusted HR = 6.8, 95% CI = 2.2 to 21.4). The risk of pleural mesothelioma also increased with increasing cumulative exposure to asbestos (HR = 1.4, 95% CI = 1.0 to 1.9; p = 0.06);

- thirdly, a panel of experts (representatives of social services, universities and scientific societies) will be set up. This multi-agency team will collect and compare the different experience developed, the definition of the operative tools, the protocols and the outcome evaluation.

Discussion

The usefulness of LDCT to identify early lung cancer in subjects with past asbestos exposure is still uncertain and definitive evidence is expected in the years to come. Indeed, the positive predictive value of LDCT is quite low, and high radiation doses are required. A recent article (13) summarized the main aspects and the initial results of the experiments with Randomized Controlled Trials currently underway on the effectiveness of LDCT as a screening test for lung cancer. According to the author of the review, although the preliminary results of the National Lung Screening North American Trial are encouraging, it is necessary to wait for the final results which will be announced over the next few years to determine whether screening for lung cancer by LDCT must be considered a public health "imperative".

In the meantime, the previously described fields of action could help to achieve the following outcomes:

- a reliable method to identify former asbestos workers;
- an evidence-based national protocol for health surveillance of asbestos workers;
- quantification of asbestos lung burden in lung cancer cases and in a local reference population.

These studies will: support the Regions in designing policies of health care designed for a category of workers who experienced inappropriate occupational exposure to asbestos and thus deserve adequate attention by the NHS; enable the various Italian Regions and the ASLs to appropriately deal with claims by asbestos workers, following guidelines taking into account scientific evidence, cost-benefits, social expectations and current regulations; offer consistent and validated protocols for care, support and medico-legal assessment to individuals whose occupational disease would otherwise likely remain neglected.

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