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HEAD & NECK

Systematic screening for occupations and occupational exposures in head and neck squamous cell carcinoma patients

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Abstract

Purpose The importance of occupational exposures in patients with head and neck squamous cell carcinomas (HNSCC) has received little attention.

Methods In a single-center study, we prospectively characterized occupational exposures in 154 HNSCC cancer patients in a systematic occupational consultation and examined the association between most frequent exposures, HNSCC stage and localization.

Results Patients occupied a mean of 3.3 different positions during their working life. The prevalence of asbestos, the most frequent exposure (46 patients; 29.9%) was higher than in the French population > 50 years. Other frequent exposures were solvents ($n=26$; 16.9%) and silica ($n=19$; 12.3%). For 37 patients (24%) a possible link was identified between occupational exposures and HNSCC. Duration of asbestos exposure was significantly higher ($p=0.04$) in patients with hypopharyngeal and laryngeal cancer compared to other localizations.

Conclusions Occupational exposures are frequent in patients with HNSCC and should receive increased attention by physicians.

Keywords Head and neck squamous cell carcinoma · Occupational exposure · Environmental exposure · Asbestos · Professional disease

Introduction

Head and neck squamous cell carcinoma (HNSCC) represent the sixth most common cancer type resulting in near 360,000 annual deaths worldwide [1]. Tobacco smoking and alcohol consumption are well established major risk factors for these cancers [2], with an increased risk of developing a HNSCC for combined use of tobacco and alcohol[3]. Second hand smoking is also an established risk factor [3]. Furthermore, infection with high-risk human papillomaviruses (HPVs) has recently been implicated in the pathogenesis of HNSCC [4]. In France, tobacco and alcohol consumption are highest among deprived patients [5], and low socioeconomic level of income and education are associated with more than two-fold increased risk of head and neck cancer [6]. Yet, HNSCC risk is not completely explained by differences in the distributions of behavioral risk factors for these cancers [6].

Several studies have investigated the role of occupational exposures in the occurrence of head and neck cancers.

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Asbestos has been shown to increase the risk of upper aerodigestive tract squamous cell carcinoma [7], in particular laryngeal and pharyngeal carcinomas as reported by recent meta analyses [8, 9]. Nickel exposure during smelting operations also has been associated with laryngeal cancer [10], as well as several other carcinogens, such as wood dust [11], sulfuric acid [12], coal products [13] or solvents [8, 14].

Occupational cancers are largely under-reported and undercompensated due to limited knowledge about occupational exposures among physicians [15] and generally, there is a lack of interest and time to collect occupational history in cancer patients [16]. The stigma associated with smoking [16], the long latency and changes in exposure patterns over time, are barriers both at physician and patient levels. Furthermore, patients in the most frequently-exposed socio-professional categories often overlook job-related exposures [17, 18].

In France, HNSCC are not covered by the list of occupational diseases assumed to be work-related when the patients meets the required medical, occupational and administrative conditions [19]. Outside the list of occupational diseases, patients' compensation claims are examined by a regional committee for recognition of occupational disease (CRRMP), who bases its assessment on the list of IARC (International Agency for Research on Cancer) Group 1 carcinogens and sufficient evidence for a causal link with disease. The CRRMP further takes into account non-occupational factors, in particular smoking [20]. In addition, patients with asbestos-related cancers, including laryngeal cancers, exposed to asbestos can make a claim to the asbestos victim compensation fund [French Fonds d'Indemnisation des Victimes de l'Amiante, FIVA (http://www.fiva.fr/)].

Thus far, little is known on the prevalence of occupational exposures, in particular asbestos exposure in HNSCC cancer patients from the general population. The aim of this prospective cohort of HNSCC patients was to assess the prevalence and features of occupational exposures in HNSCC cancer patients and to examine whether the prevalence of exposure to carcinogens differed between primary tumour sites.

Materials and methods

The present research was a prospective study to investigate the prevalence and features of occupational exposures in patients with head and neck squamous cell carcinomas prior to the implementation of a systematic screening of occupational exposures in this population in the Léon Bérard cancer center [18].

The study was declared to the National Committee for Protection of Personal Data (n°2,062,434) and was approved by the Ethics Committee of the Regional Comprehensive Cancer Center Léon Bérard (CLB), Lyon, France.

Study population

Patients (male and female with no age limitation) referred to the CLB for their first head and neck squamous cell carcinoma between the 1st of January 2009 and the 1st of July 2011, speaking French language, and without previous personal medical cancer history were eligible. All eligible patients were offered by their head and neck surgeon to benefit from a supplementary occupational cancer consultation during the consultation to announce the diagnosis. After giving their consent, patients were given an appointment that did not delayed the diagnostic or therapeutic process. Patients managed elsewhere or referred only for radiotherapy, diagnostic procedures, or second medical opinion were not eligible.

Occupational cancer consultation

During the consultation, one of the two physicians specialised in occupational and environmental health, collected data on the patient's job history, exposure to carcinogens, conditions, frequency, duration and level of exposure, means of protection and non-work-related risk factors (i.e. smoking history and non-occupational exposure, in particular to asbestos).

Data collection

For each patient, the complete job history (job-title, start and end dates for each job held (work period), employer and sector of activity, and tasks performed), exposure to carcinogens (conditions, frequency, duration and level of exposure; means of protection) as well as non-work-related risk factors (i.e., smoking history, alcohol consumption, non-occupational exposure, in particular to asbestos) were collected by the physician. All consultations were registered in the database of the National Network for Monitoring and Prevention of Occupational Diseases [21].

Assessment of occupational exposure

Work periods (WP), defined as a time interval during which the patient has occupied the same job in the same sector, were collected for every patient.

The jobs and sectors were encoded by an occupational health physician using the International Standard Classification of Occupations (ISCO-08) of the International Labour Organisation (ILO) [22], the French Classification of Occupations and Socio-professional categories (PCS 2003) [23] and the French Nomenclature of Activities classification (NAF 2008) [24].

The level of imputability was assessed taking into account the patient's personal history of occupational

exposures and estimation of the level and duration of exposures, the latency period, the scientific evidence from the literature and the IARC classification, and the existence of non-occupational factors related to the disease. The imputability was classified: 0 (very unlikely, no imputability); 1 low imputability; 2 medium imputability or 3 high imputability.

Statistical analysis

Data were analysed using descriptive statistics, t-tests and Mann–Whitney tests for comparisons of quantitative data and Chi-square and Fisher exact tests for qualitative data. All enrolled patients were included in the analysis.

Results

Between January 2009 and July 2011, 154 patients with HNSCC were referred to our institution, including 125 men (81.2%) and 29 women (18.8%). No patient refused to participate in the present study.

Table 1 Patients' characteristics

	N	%
Gender		
Men	125	81.2
Women	29	18.8
Current/former smoker		
No	19	12.6
Yes	132	87.4
1 to < 20 pack-years	18	11.9
20 to < 40 pack years	32	21.2
≥ 40	82	54.3
Current/former alcohol drinker		
No	21	13.6
Yes	133	86.4
Occasional (0–5 units/week)	19	12.4
Excessive (> 5 units/week)	114	74

Three patients presented with two synchronous HNSCC tumours leading to an overall number of 157 tumours.

Characteristics of the patients and the tumours

The patients' characteristics are summarized in Table 1. Most patients (87.4%) were smokers (current/ex-smokers), and only 13.6% of patients had no daily alcohol consumption. The majority of patients were diagnosed with a stage IV disease (45.4%) (Table 2). Mean age at diagnosis was 62 (standard deviation 10.25) years. Primary tumours sites and tumour stages are presented in Table 2.

Socio-professional categories

All patients attended the consultation. Most patients reported several successive occupations (Table 3) and socioprofessional categories (Table 4) during their career. Therefore, the total is superior to the number of patients. All patients reported at least 1 work period (WP), with a mean of 3.3 (std. 1.4) WPs. Most patients reported several successive occupations and socioprofessional categories during their career. Therefore, the total is superior to the number of patients. The mean total work duration was 27.2 (std. 12.0) years. Distribution of occupational sectors are presented in Table 3. Manufacturing (87 WPs overall), automobile retail and repair (47 WPs) and construction (42 WPs) were the most frequent occupational sectors. Craft and related trades workers (75 WPs) and plant and machine operators and assemblers (49 WPs) were the most frequent socioprofessional categories. Overall, 75 patients (48.7%) were artisans or craft workers, with a mean work duration of 22.2 years. There was no difference in the distribution of tumour stage at diagnosis among socio-professional categories (Mann–Whitney test).

There was a significant difference in the distribution of primary tumour sites among "services and sales workers" and among "craft and related trades workers" (Table 5), for several occupational sectors although tobacco and alcohol consumption in those groups was not different from other groups.

Table 2 Tumour characteristics

Primary tumour site	TOTAL	Stage 0/1 (*n* = 33)		Stage 2 (*n* = 31)		Stage 3 (*n* = 23)		Stage 4 (*n* = 70)	
	N	*N*	%	*n*	%	*n*	%	*N*	%
Oral cavity	67	17	51.5	10	32.3	12	52.2	28	40
Oropharynx	33	3	9.1	6	19.3	4	17.4	20	28.6
Hypopharynx	21	1	3	3	9.7	3	13	14	20
Larynx	36	12	36.4	12	38.7	4	17.4	8	11.4
Total	157	33	100	31	100	23	100	70	100

Table 3 occupational sector for 154 patients

Occupational sector (NAF 2008)	*N* (%)
Agriculture, fishing and forestry	13 (8.4)
Mining and quarrying	1 (0.6)
Manufacturing	79 (51.3)
Electricity, gas supply	2 (1.3)
Water supply	1 (0.6)
Construction	40 (26)
Retail, automobile repair and domestic appliances	42 (27.3)
Hotels et restaurants	22 (14.3)
Transportation	27 (17.5)
Communication information	3 (1.9)
Financial activities	4 (2.6)
Realty, rental, and business services	3 (1.9)
Public Administration	8 (5.2)
Education	8 (5.2)
Human health and social work	29 (18.8)
Collective, social, and personal services	6 (3.9)
Activities of households as employers of domestic staff	9 (5.8)
Art, entertainment and leisure	2 (1.3)
Other services activity	7 (4.5)
Activities of households as employers; undifferentiated goods- and services-producing activities of households for own use	3 (1.9)
Occupational sectors, total*	309 (100%)

*Frequencies of occupational sectors and socio professional categories exceed 100% because patients reported several successive occupations and socioprofessional categories during their career

Table 4 Socio professional categories for 154 patients

Socio professional categories (ISCO 08)	*N* (%)
1. Managers	28 (18.8%)
2. Professionals	23 (15.9%)
3. Technicians and associate professionals	32 (20.8%)
4. Clerical support workers	20 (13%)
5. Services and sales workers	31 (20.1%)
6. Skilled agricultural. forestry and fishery workers	9 (5.8%)
7. Craft and related trades workers	75 (48.7%)
8. Plant and machine operators and assemblers	49 (31.8%)
9. Elementary occupations	30 (19.5%)
10. Armed forces occupations	6 (30.9%)
Socio professional categories, total*	303 (100%)

*Frequencies of occupational sectors and socio professional categories exceed 100% because patients reported several successive occupations and socioprofessional categories during their career

Occupational exposures

Overall, at least one occupational exposure was identified

Table 5 Occupational characteristics according to primary tumour site

In years of exposure	All $n=157$			Oral cavity (C0–C08) $n=67$			Oropharynx (C09–C10) $n=33$			Hypopharynx (C12–C14) $n=21$			Larynx (C32) $n=36$			*p* value (Mann–Whitney)
	n	Mean (std)	Sum	*n*	Mean (std)	Sum	*n*	Mean (std)	Sum	*n*	Mean (std)	Sum	*n*	Mean (std)	Sum	
ISCO 08 Major Groups																
1 Managers	28	17.6 (12.1)	491.5	15	15.3 (11.7)	230	7	21.6 (13.4)	151	2	22.3 (17.3)	44.5	4	16.5 (12)	66	0.7
2 Professionals	23	21.1 (13.6)	484.5	10	28.2 (11.2)	281.5	8	17.1 (12.6)	136.5	1	40 (0)	40	4	6.6 (2.9)	26.5	–
3 Technicians and associate professionals	33	19 (13.3)	627.5	17	21.5 (13.2)	366	10	15.9 (14.4)	158.5	2	14.3 (15.9)	28.5	4	18.6 (12.8)	74.5	0.6
4 Clerical support workers	20	22.4 (15.7)	448.5	9	29.1 (12.5)	261.5	6	18.8 (19.2)	113	1	15.5 (0)	15.5	4	14.6 (16.2)	58.5	–
5 Services and sales workers	31	15.7 (13.3)	486	15	18.7 (13.6)	280.5	7	4.9 (2.3)	34.5	3	20.3 (19.3)	61	6	18.3 (13.6)	110	0.02
6 Skilled agricultural. forestry and fishery workers	11	21.4 (16.3)	235.5	6	25.6 (17.7)	153.5	2	12.3 (1.1)	24.5	2	7.8 (3.2)	15.5	1	42 (0)	42	–
7 Craft and Related trades workers	77	21.7 (14.4)	1670.25	26	15.8 (13.3)	410.25	16	19.5 (13.4)	312.5	15	26.5 (16.6)	397.5	20	27.5 (12.1)	550	0.02
8 Plant and machine operators and assemblers	49	15.7 (14)	768.5	17	12.4 (14.4)	210.5	10	17.4 (12.2)	174	6	25.7 (16.5)	154	16	14.4 (13.3)	230	0.2
9 Elementary occupations	30	13.9 (10.8)	415.5	14	13.3 (8.1)	186	3	10.7 (13.7)	32	4	17.1 (15.8)	68.5	9	14.3 (12.9)	129	0.8
0 Armed forces occupations	6	2.2 (0.9)	13	3	2 (1)	6	2	2.5 (1.4)	5	0	0 (0)		1	2 (0)	2	–

in 102 patients (66.2%) and a total of 54 different exposures were identified in our population (Table 6). The mean number of occupational exposures per patient was 1.9 (std. 2.0). The mean number of occupational exposures among patients with at least 1 exposure was 2.9 (std. 1.9). The three most frequently reported occupational exposures (Table 6) were asbestos, identified for 46 patients (29.9%) with a mean exposure duration of 15.7 years (std. 12.1), solvents (26 patients; 16.9%); mean exposure duration 8.9 years, and silica (19 patients; 12.3% ;mean exposure duration 15.9 years). Occupational exposures according to the primary tumour site are presented in Table 5.

Occupational asbestos exposure

Overall, 46 patients (29.9%), corresponding to 47 primary tumour sites, had an occupational exposure to asbestos; 98% were men. There was no significant difference in tumour stage between asbestos-exposed patients and patients without asbestos exposure. There was no difference in tobacco consumption between patients exposed to asbestos and other patients, however, alcohol consumption was significantly higher in asbestos-exposed patients. Also, the average number of occupational exposures was higher in patients exposed to asbestos compared to non-exposed patients (mean = 3.74, std = 2.34) and 3.12 occupational exposures (std = 1.66) respectively (p = 0.06). Furthermore, patients exposed to asbestos were significantly more often exposed to acids (10.9 vs. 2.8, $p = 0.04$), glues (6 vs. 0, $p = 0.007$), welding fumes (17.4 vs. 2.8, $p = 0.003$) and silica (28.3 vs. 4.6, $p < 0.0001$). Duration of asbestos exposure was significantly higher ($p = 0.04$) in patients with hypopharyngeal and laryngeal cancer compared to other localizations. In the hypopharyngeal SCC group, the prevalence of asbestos exposure was significantly higher (12/21 patients = 60, $p = 0.02$), with a longer mean exposure duration (18.2 years) compared to all other primary tumour sites. Among them, one patient had no alcohol consumption and little tobacco exposure (10 pack-years).

Non-smoker and non-drinker patients

Overall, 9 patients (5.8%, 6 women and 3 men) were non-smokers and non-drinkers. The proportion of women was higher than in the overall population. Three of the 9 patients were exposed to solvents and one patient was exposed to asbestos.

Level of imputability

Taking into account scientific evidence and the IARC classification of carcinogens, the disease was considered imputable to occupational exposures in 37 patients (24%), and for 2 patients (1.3%) a possible environmental origin of the disease was identified; among them the level of imputability was found low in 31 patients (20.1%) medium in 6 patients (3.9%) and strong in 2 patients (1.3%) the remaining 115 (74.7%) patients were considered to have neither work- nor environmentally related HNSCC.

A claim for compensation was judged possible under the French system for 4 patients (2.6%) and the mandatory medical certificate was delivered to 2 patients. Finally, 1 patient had his disease recognized as a professional disease.

Discussion

To our knowledge, this is the first study to characterize occupational exposures in HNSCC patients from the general population attending a comprehensive cancer center in France. The strength of this study includes the systematic occupational cancer consultation with a specialised physician for all patients newly referred to the center. Because patients with a low socio-economic status are known to experience greater difficulties with administrative processes [16, 25], all patients were given the appointment by their surgeon after an explanation about its purpose, without having to go through any particular formalities. All patients accepted to meet the occupational health practitioner.

Data collected on HNSCC patient's job history reflect the low socio economic status usually associated with HNSCC patients, despite patients attending the French comprehensive cancer centers may have a higher socio-economic status compared to the general population. Compared to data for the French active population in 2010 [26], economic sectors such as agriculture, construction and industry are over-represented in our HNSCC population. This number may be linked to the social fragility of these patients who often held and may accumulate precarious employments Finally, occupational status was not associated with the stage or the primary tumour site of HNSCC in our study, which is concordant with other observations made by Adrien and al [27].

The proportion of exposed patients in our study largely exceeded the proportion of 13,7% and 10,4% of employees estimated to be exposed to occupational carcinogens respectively in 2003 and 2010 in the French general population [28]. On average, our study population was exposed to 1.91 hazardous substances, and 2.88 in patients with at least one occupational exposure, which is higher than what is observed in the general working population at the same period [29]. However, while our study allowed comparisons with exposure rates in the general population, the statistical power was limited for subgroup analyses.

Table 6 Occupational exposures according to the 157 primary tumour sites

	Total ($n=157$)		Oral cavity ($n=67$)		Oropharynx ($n=33$)		Hypopharynx ($n=21$)		Larynx ($n=36$)	
	n	%	*n*	%	*n*	%	*n*	%	*n*	%
Exposure										
Aluminium	1	0.6							1	2.8
Asbestos	47	29.9	12	17.9	14	42.4	12	57.1	9	25.0
Amino amides	0									
Benzene	1	0.6					1	4.8		
Chlorine	1	0.6	1	1.5						
Vinyl chloride	2	1.3					1	4.8		
Chromates	0									
Copper	1	0.6							1	2.8
Cyanide	1	0.6					1	4.8		
Detergents	1	0.6	1	1.5						
Thinners	0									
Ink	0									
Flocculants	0									
Formaldehyde	2	1.3	2	3.0						
Freon	1	0.6	1	1.5						
Frying	5	3.2	3	4.5			1	4.8	1	2.8
Graphite	1	0.6	1	1.5						
Polycyclic aromatic hydrocarbon	5	3.2			1	3.0			4	11.1
Cutting oil	13	8.3	5	7.5	2	6.1	2	9.5	4	11.1
Hydraulic oils	1	0.6			1	3.0				
Bleach	0									
Glass elder	3	1.9	2	3.0			1	4.8		
Plastic materials	1	0.6	1	1.5						
Sintered metal	1	0.6	1	1.5						
Polyurethane foams	1	0.6	1	1.5						
Nickel	0									
Carbon black	4	2.5			2	6.1			2	5.6
Radiofrequency waves	1	0.6	1	1.5						
Pesticides	4	2.5	1	1.5	1	3.0			2	5.6
Lead	1	0.6	1	1.5						
Wood dust	13	8.3	4	6.0	1	3.0	3	14.3	5	13.9
Cardboard dust	1	0.6							1	2.8
Leather dust	3	1.9					1	4.8	2	5.6
Flour dust	2	1.3					1	4.8	1	2.8
Plaster dust	0									
Textile dust	1	0.6	1	1.5						
Hair product	1	0.6							1	2.8
Cleaning produts	3	1.9	3	4.5						
Epoxy resins	0								1	2.8
Silica	19	12.1	5	7.5	4	12.1	5	23.8	5	13.9
Caustic soda	1	0.6					1	4.8		
Passive smoking	5	3.2	4	6.0	1	3.0				
Shoe dye	1	0.6	1	1.5						
Wood preservative	1	0.6	1	1.5						
Solvent	26	16.6	10	14.9	5	15.2	4	19.0	7	19.4
Paint	8	5.1	3	4.5	3	9.1			2	5.6
Fumes	3	1.9	2	3.0	1	3.0				
Welding fumes	11	7.0	3	4.5	2	6.1	1	4.8	5	13.9

Table 6 (continued)

	Total ($n=157$)		Oral cavity ($n=67$)		Oropharynx ($n=33$)		Hypopharynx ($n=21$)		Larynx ($n=36$)	
	n	%	*n*	%	*n*	%	*n*	%	*n*	%
glue	3	1.9					2	9.5	1	2.8
Acids	8	5.1	2	3.0	1	3.0	2	9.5	3	8.3
Hydrocarbon	4	2.5	1	1.5	2	6.1			1	2.8
Ionising radiation	4	2.5	4	6.0						
Metal dust	6	3.8	1	1.5			1	4.8	4	11.1
House dust	7	4.5	2	3.0			1	4.8	4	11.1

Despite its prohibition in France since 1997, asbestos was the predominant occupational carcinogen identified in the present study. The lifetime prevalence of occupational asbestos exposure of 42,5 in our study exceeded asbestos exposure of men aged over 50 in the French general population, estimated around 30% in 2007 [7, 30]. Moreover, 25% of patients with laryngeal cancer were exposed to asbestos. Asbestos is classified as carcinogenic for humans (group 1) and the IARC concluded in 2009 on sufficient evidence that asbestos exposure causes laryngeal cancer and limited evidence for pharyngeal cancer [7]. The fraction of laryngeal cancer attributable to occupational asbestos exposure in France is estimated between 4.5% and 25.6% in men and 0.5% and 1.7% in women, depending on the scenarios [31]. Furthermore, the duration of asbestos exposure was significantly higher in patients with hypopharyngeal and laryngeal cancer compared to other localizations, and the prevalence of asbestos exposure was significantly higher than in other primary tumour sites. These observations are consistent with data from a French case–control study reporting significant increased risk of hypopharyngeal cancer (OR = 1.80, 95 CI 1.08–2.99) and a nonsignificant increased risk of laryngeal cancer (OR = 1.24, 95 CI 0.83–1.90) associated with asbestos, after adjustment for tobacco and alcohol comsumption [32]. Our study is the first study investigating asbestos exposure in HNSCC according to the cancer stage. We did not find any significant association between asbestos exposure and HNSCC stage, while we found a significant association of the level of tobacco or alcohol use and the stage of the disease.

Solvent exposure was the second most frequent occupational exposure in the study population. Exposure to solvents has been found to be associated with oral and pharyngeal or laryngeal and hypopharyngeal cancer risk by several studies, although others did not find an association [14, 33, 34]. Some solvents such as trichloroethylene (TCE) [35], tetrachloroethylene (PCE) [36] are classified by IARC as carcinogenic or probably carcinogenic to humans, but for cancer sites other than HNSCC. Vaughan et al. found a non-significant increased risk of oral, pharyngeal, and laryngeal cancer among subjects exposed to PCE and Barul et al. [37], based on a French population based case–control study, reported a non-significantly increased risk of laryngeal cancer associated with high PCE exposure, and suggested an association between exposure to methylene chloride and hypopharyngeal cancer. Silica was the third most frequently detected occupational exposure in our study. Chen et al. reported evidence for an association of laryngeal cancer with silica dust, although only the pooled risk from case–control studies was statistically significant [32]. Paget-Bailly et al. reported a non-significantly elevated risk for the highest level of cumulative silica exposure for oropharyngeal (OR = 1.6 CI 0.8–3.2) and hypopharyngeal cancer (OR = 1.9 CI 0.9–4.1) in the French ICARE study [38].

Finally, the imputability of the disease to professional exposures was found possible for 24% of our patients, and high or intermediate for 5.2% of all patients. However, while patients with asbestos-related lung cancer and mesothelioma matching medical and exposure conditions can ask for compensation in many countries, the possibility of recognition and compensation of asbestos-related laryngeal and hypopharyngeal cancers remains limited in our country.

Conclusion and perspectives

Our study confirms the frequency of occupational exposures among patients with HNSCC, and a predominance of craft and related trades socioprofessionel categories in this population. Physicians should be aware of the possible causal connection between HNSCC and asbestos exposure and ask for occupational exposures more systematically, in particular in patients with low tobacco consumption.

However, despite the imputability of environmental or occupational factors has been found possible for 24% patients, only one patient had his disease finally recognized as a professional disease ; therefore, the results of this study did not lead us to generalize a systematically screening such as the one decided for lung cancer [18].

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