

Original Article

Occupational Burden of Cancer in Korea

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Objectives: The extent of the occupational cancer burden has rarely been estimated in Korea. The aim of this study is to provide an estimation of the population attributable fraction (PAF) of occupational cancer in Korea.

Methods: Nine kinds of Group 1 carcinogens addressed by the International Agency for Research on Cancer (IARC) and 7 kinds of cancer were selected for the target carcinogens and diseases, respectively. The prevalence of carcinogen-exposed workers was estimated and correction factors were applied so that the value would be representative of the total population. Data on relative risk (RR) were taken from IARC reports and were compared with the RRs from the studies on Korean workers. The PAF was estimated according to Levin's formula.

Results: The proportion of the general Korean population exposed to carcinogens was 9.7%. The PAF of total cancer was 1.1% for incident cancer cases and 1.7% for cancer deaths. The PAFs of lung cancer and leukemia were 7.0% and 4.5%, respectively. With the RRs reported from Korean studies, the PAF for lung cancer and leukemia were 3.7% and 3.4%, respectively.

Conclusion: The PAF in this study (1.1%) was lower than that reported in previous studies (2-4%) from developed countries. Considering that only 9 of the 29 kinds of Group 1 carcinogens were included in this study, the PAF might be underestimated. However, because the process of industrialization in Korea differs from that which occurred in other developed countries, 1.1% of the PAF might be appropriate for Korea.

Key Words: Exposure prevalence, Epidemiologic investigation, Occupational cancer, Population attributable fraction

Introduction

Cancer is the most prevalent cause of death in Korea; the cancer mortality rate in 2008 was 141.1 per 100,000 person-years [1]. Occupational environment has been regarded as one of the most significant and preventable causes of cancer. The global burden of occupational cancer was first estimated in 1981 at 2-4% of total cancer cases [2]. Several studies from Western Europe [3] and Nordic countries [4] were subsequently conducted to determine the population attributable fraction

(PAF) of occupational cancer, reporting a range of 2.0-13.8%.

In Korea, heavy and chemical industries underwent rapid growth during the 1970s. The first occupational cancer was mesothelioma due to asbestos, reported in 1993 [5]. The Occupational Safety and Health Research Institute (OSHRI) of the Korea Occupational Safety and Health Agency (KOSHA) has conducted epidemiologic investigations and research on occupational cancer since 1992. These investigations were requested by the Korea Workers' Compensation and Welfare Service (KOMWEL) for clarification of compensation issues. These investigations showed that various kinds of occupational cancers, such as mesothelioma, lung cancer, leukemia, non-Hodgkin's lymphoma, and bladder cancer, have appeared since 1992 [6-9].

However, only one attempt has been made to estimate the occupational burden of cancer in Korean workers [10]. Estimation of the PAF requires detailed information, such as

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the national incidence of cancer, the proportion of workers exposed to carcinogens, and the relative risk (RR) of a specific carcinogen. Such data have been lacking or inadequate in previous years.

The first report of the national incidence of cancer in Korea appeared in 1998, and the incidence rates of all kinds of cancer have been reported since 2002 [11]. The first estimation of national cancer incidence relied on many kinds of resources that had been published by the Cancer Registration Statistics Program of the Ministry of Health and Welfare [11]. The proportion of carcinogen-exposed workers was measured in a nationwide survey, first conducted in Korea in 1994, on chemical utilization in the workplace. Because the quantity of research has increased since 2000, the RRs of specific carcinogens in Korean workers were not calculated in the original survey.

Using the data from the 1999 survey of workers in the manufacturing industries, Cho et al. [10] estimated that the annual count of occupational cancers is 5 to 28 cases based on the proportion of the workers exposed to 9 carcinogens. However, this is likely to be an underestimation because the calculation of exposed workers included only salaried workers in manufacturing sectors.

Efforts have been made to obtain more information on the prevalence of carcinogen-exposed workers in Korea. The Korean Statistical Information Service (KSIS) has published the number of workers by industrial sectors from 1993 [12]. Additionally, several epidemiologic studies have been conducted on those working with benzene [13,14], asbestos [15], carcinogenic metals [16], radiation [17], and iron and steel [18], and on those working in mines [19,20] and foundries [21], reporting the RR and exposure prevalence for each carcinogen.

The aim of this study was to provide an estimation of the PAF of occupational cancer in Korea based on recent estimations of the prevalence of exposure.

Materials and Methods

The methodology involves four main steps: 1) selecting the occupational carcinogens and target cancers; 2) estimating the prevalence of exposure at any time in the workforce for the carcinogens of interest; 3) estimating the magnitude of RR associated with the carcinogens of interest; and 4) estimating the attributable fraction of cancer attributed to occupational exposure using Levin's formula [22].

In our study, most information used to calculate the prevalence of carcinogen-exposed workers was from the manufacturing and mining industries. Information about

occupational cancers from primary industries such as agriculture, forestry and fisheries, the public sector, the military service, and private schools was not included.

Selection of occupational carcinogens and target cancers

To select the major occupational carcinogens and the target cancers among IARC Group 1 carcinogens [23], the authors reviewed occupational cancers from epidemiologic investigations conducted by OSHRI of KOSHA. The authors reviewed 110 occupational cancer cases from 1992 to 2008 (Table 1). Lung cancer, leukemia, and mesothelioma were the most commonly reported occupational cancers. With one exception, all cases of mesothelioma were thought to be related to asbestos exposure. The main carcinogens for respiratory cancers were asbestos, silica, chromium, and nickel. Polycyclic aromatic hydrocarbons (PAHs) have also been reported to cause respiratory cancers. The biggest cause of lymphohematopoietic

Table 1. Occupational cancer cases from epidemiologic investigation of OSHRI, KOSHA

	Causal carcinogens	Work-related cases
Respiratory system		71
Lung	Asbestos, crystalline Silica, diesel exhaust, chromium and cadmium, nickel, PAH	67
Larynx	PAH	2
Nasopharynx	Chromium, PAH	2
Malignant mesothelioma	Asbestos	13
LHP system		22
Leukemia	Benzene, radiation, anticancer drug	16
Malignant lymphoma	Benzene	6
Urologic system	-	
Bladder	Benzidine and benzidine based dye	3
CNS	Methylene chloride	1
Total		110

OSHRI: Occupational Safety and Health Institute, KOSHA: Korea Occupational Safety and Health Agency, PAH: polycyclic aromatic hydrocarbon, LHP: lymphohematopoietic, CNS: central nervous system.

cancers was benzene; however, three cases of ionizing radiation were reported. Bladder cancers reported in three cases were caused by benzidine. Even if central nervous system cancer was work-related, methylene chloride was not regarded as a confirmed occupational carcinogen from IARC, and so the authors did not include central nervous system cancers for analysis. Anticancer drugs causing leukemia and diesel exhaust causing lung cancer were also not included for occupational cancer analysis because no appropriate epidemiologic studies had been conducted of the exposed population.

From this review, 9 carcinogens (ionizing radiation, asbestos, crystalline silica, wood dust, cadmium and cadmium compounds, hexavalent chromium compounds, nickel compounds, benzidine or benzidine dehydrochloride, and PAH) and 7 kinds of cancers (lung cancer, laryngeal cancer, leukemia, non-Hodgkin's lymphoma, malignant mesothelioma, bladder cancer, and sinonasal cancer) were selected for analysis. The specific industries classified by the IARC as Group 1 were excluded because the relevant agents were already included (for example, coke production as PAH, boot and shoe manufacture as benzene, painting as benzene, rubber industries as benzene, iron and steel foundries as silica).

Eight carcinogens (shale oils, soot, bis (chloromethyl) ether and chloromethyl methyl ether, 4-aminobiphenyl, 2-naphthylamine, 2,3,7,8-tetrachlorodibenzo-para-dioxin (TCDD), aflatoxin, and mustard gas) were not regarded as important occupational carcinogens in Korea. Data for 12 carcinogens (formaldehyde, coal tar pitch, solar radiation, erionite, talc containing asbestiform fibers, arsenic and arsenic compounds, beryllium, vinyl chloride, ethylene oxide, strong inorganic acid mists, mineral oil and involuntary smoking) are currently unavailable. However, coal tar pitch might be regarded as the main PAH to which the Korean population has been exposed, and PAH was selected as the main target carcinogen.

Prevalence of workers' exposure to occupational carcinogens

Given the considerable time it takes for cancer to develop (usually at least 10 years), the proportion of carcinogen-exposed workers was estimated based on data from 1995.

The number of the workers exposed to cadmium [13], chromium [13], nickel [13], asbestos [24], and benzidine [9] in 1995 was estimated from separate research on those topics. Because of a lack of information, the number of workers exposed to cadmium, chromium, and nickel was estimated using the number of workers in 2000. These studies represented 0.68 million workers receiving specific medical monitoring for

specific risk factors.

For other carcinogens, such as PAH, silica, wood dust, benzene, and leather, the number of workers exposed in 1995 was estimated based on data from the KSIS national survey of workers in the mining and manufacturing industries from 1995 to 2005 [12]. Approximately 4.3 million workers from the manufacturing and mining industries participated in the KSIS survey.

The economically active population in 1995 was 20.8 million. The above numbers notably excluded workers who were not covered by specific medical monitoring, were in various other industries, or were unemployed (Table 2).

The following process was adopted to adjust for this bias, in accordance with the IARC report on attributable causes of cancers in France [25]:

Step 1: The exposed proportion of workers was calculated for each carcinogen using the denominator obtained from the information source.

Step 2: The workers not covered by specific medical monitoring (3.6 million) (Table 2) could have been exposed to carcinogens, even though the exposure level was at a relatively lower level than that of medically monitored workers. In general, specific medical monitoring for carcinogens was conducted on relatively highly exposed workers who were selected by an industrial hygienist in accordance with the Occupational Safety and Health Act in Korea. The proportion of exposed workers was lower among workers not receiving medical monitoring than among those who did. Therefore, we applied half of the occupational exposure prevalence estimated in Step 1 to this population.

Table 2. Population of Korea in 1995 (unit: million)

Substance or mixture	'95
General population	44.55
Economically active population	20.85
Employed workers	17.99
Mining & manufacturing	4.31
Workers receiving medical monitoring	0.68
Workers not receiving medical monitoring	3.64
Other industries	13.7
Unemployed workers	2.86
Aging population > 65 years old	2.64

Step 3: Of the workers in the study, 13.7 million were from industries other than manufacturing or mining (Table 2). Although carcinogen exposure was possible in this population, the extent of exposure was much less than in miners and workers in the manufacturing industry. We applied one-fourth of the prevalence estimated in Step 1 to this population.

Step 4: Among the economically active population, 2.9 million were unemployed. Because this population could have been exposed during an occupation before their unemployment period, unemployed workers were considered to have an occupational exposure prevalence equal to one-fourth of the prevalence estimated in Step 1.

Step 5: The 2.6 million participants who were over the age of 65 years (Table 2) might have had a past exposure that was higher than their current one. To account for the secular decrease in exposure to occupational carcinogens, we applied a correction factor of 1.25 to the prevalence of occupational exposure computed for the overall economically active population (steps 1-4).

Step 6: The prevalence from step 1 was derived from cross-sectional studies. This focused only on the last job held. Hence, for estimation of the prevalence of lifetime occupational exposure, a factor of 4 was applied, based on the report about the lifetime occupation turnover rate from the Korea Employment Information System [26].

Exposure to ionizing radiation occurs in special industries that are strictly controlled by the Korea Radioisotope Association (KRA). The population exposed to ionizing radiation was estimated from the numbers of industries using radioisotopes, as supplied by KRA statistics [27], and multiplying the average number of workers without applying the correction factor.

Relative risk of occupational cancers

The authors reviewed the IARC RRs that were taken from a French report conducting PAF analysis [25] and another systematic review article on global estimates of the burden of occupational cancer by Driscoll et al. [3]. The authors also reviewed reports on occupational cancers in Korea since

Table 3. Relative risk of occupational cancers by specific carcinogens in Korea and IARC

		Korea	Reference	IARC	Reference
Lung	Asbestos	'00-04, exposed: 3.48 '83-'06, textile: 7.0	[16] [15]	1.48	[25]
	Cadmium	-		1.17	[25]
	Chromium	'00-'02: 1.48	[13]	3.1	[25]
	Nickel	-		1.8	[25]
	Crystalline silica	'97-'00, miner: 1.1-1.3 foundry: 1.3	[20] [21]	1.2	[25]
	PAH	'88-'02, steel: 1.9	[18]	1.37	[25]
Mesothelioma	Asbestos	*		*	
Nasal cavity & sinus	Chromium	-		5.18	[25]
	Nickel	-		2.09	[25]
	Wood dust			0.8-5.8	[25]
	Leather			1.3-2.7	[25]
Leukemia	Benzene	'88-'05: 1.82-2.71	[14]	3.3	[25]
	Radiation	'92-'04: 0.59	[17]	0.2	[3]
NH	Benzene	'88-'05: 1.8	[14]	-	
Lymphoma	Radiation	'92-'04: 1.26	[17]	-	
Bladder	Benzidine	-		1.6	[25]
	PAH	-		1.4	[25]

IARC: International Agency for Research on Cancer, PAH: polycyclic aromatic hydrocarbon, NH: non-hodgkin's.
*Direct calculation.

2000. A total of 8 reports, were included for review of the RR of Korean occupational cancers regarding asbestos [13,15], chromium [13,15], crystalline silica [19,20], PAH [18], benzene [14,16], and radiation [17]. As a result, the RRs for lung cancer, leukemia, and non-Hodgkin's lymphoma in Korea are available.

In Table 3, the IARC and Korean RRs are summarized. The RRs for lung cancer with asbestos ranged from 3.48 (for all industries) to 7.0 (for asbestos textile industries). The RR for lung cancer due to chromium exposure was relatively higher in the IARC reports (3.1) than in Korea (1.63).

The RR of lung cancer from crystalline silica in Korea was 1.1 to 1.3 for miners and 1.3 for workers in foundries. The RR of lung cancer from PAH in Korea was 1.9, which was lower than in the IARC reports. The RR of leukemia or lymphoma from benzene in Korea was 1.8 to 2.7. The RR of leukemia or lymphoma from radiation was 0.59 in Korea and 0.2 in other countries.

Calculation of the PAF

The PAF can be calculated as below, as the function of the RR

and the prevalence of exposure, as described by Levin [22].

$$PAF = P \times (RR - 1) / [P \times (RR - 1) + 1]$$

Where P = the proportion of the workers exposed to carcinogen

and

RR = relative risk

We used the IARC RRs to estimate the PAF. For lung cancer and leukemia, we used the Korean RRs as well. Because the RR for non-Hodgkin's lymphoma was not reported in the IARC report [25] and in the study by Driscoll et al. [3], PAF for non-Hodgkin's lymphoma was based solely on Korean RRs.

Since asbestos is a well-known cause of mesothelioma and is reported to be 80% to 90% of PAF [28], we assumed that the PAF of mesothelioma is 80% in this analysis.

To calculate the cancer counts attributed to occupation, the mortality [1] and incidence [11] of cancer in 2005 were derived from the annual reports of Korea KOSIS and the National Cancer Center of Korea, respectively. We used the 2005 statistics regarding the incidence rate of cancer in Korea because they were national in scope [11]. We calculated attributed cancer counts by multiplying the calculated PAFs by the counts of cancer deaths and incidence of each cancer.

Table 4. Estimated prevalence of lifetime occupational exposure to carcinogen in Korea

Substance or mixture	Estimated prevalence (%)*
Ionizing radiation	0.36
Asbestos	0.16
Cadmium	0.46
Chromium	3.12
Nickel compounds	0.19
Benzidine or benzidine dehydrochloride	Production 0.51 Dying 6.5
PAH	0.84
Crystalline silica	Miner 0.79 Others 0.98
Wood dust	1.75
Benzene	2.17
Leather	0.22
Total	9.66

PAH: polycyclic aromatic hydrocarbon.

*Estimated percentage of lifetime exposure among economically active population, adjusted by correction factors for kinds of industries, unemployment, private sectors and turn-over rate.

Results

Table 4 summarizes the final proportion of workers exposed to

Table 5. Population attributed fraction (PAF) of occupational cancer and the estimated number of cancer using PAF in 2005

	PAF (%)	Estimated number of cancer cases using PAF	
		Incidence	Death
Lung	7.0 (3.7)	1,181 (630)	962 (513)
Larynx	0.3	4	2
Mesothelioma*	80	60	36
Sinonasal	19.9	116	24
Leukemia	4.5 (3.4)	102.3 (78)	64.4 (49)
NH_lymphoma	(1.8)	(53.3)	(4)
Bladder	4.4	128	40
Total cancer		1,644 (1,068)	1,142 (677)
% of all cancers		1.1 (0.75)	1.7 (1.0)

NH: non-hodgkin's.

*Direct estimation, parenthesis representing the result applying relative risks from Korean studies.

occupational carcinogens. After applying correction factors described in the Methods section, the proportion of carcinogen-exposed workers among the general Korean population was estimated to be 9.7% (Table 4). The highest prevalence of exposure was to benzidine or benzidine dehydrochloride (7.0%) and chromium (3.12%). The prevalence of exposure to asbestos and benzene was 0.16% and 2.17%, respectively.

Table 5 lists the calculated PAFs for incident cancer cases and deaths using IARC and Korean RRs. In 2005, a total of 1,644 cases of cancer (1.1%) were attributed to occupation, using the IARC RRs. The PAFs of lung cancer and leukemia using the IARC RRs were 7.0% and 4.5%, respectively. The PAF of sinonasal cancer was 19.9%. With the RRs reported from Korean studies, the PAFs for lung cancer, leukemia, and non-Hodgkin's lymphoma were 3.7%, 3.4%, and 1.8%, respectively. The number of cancer deaths attributable to occupation using the IARC RRs was 1,142 (1.7%).

Discussion

We attempted to calculate the PAF of occupational cancer in Korea using the estimated proportion of carcinogen-exposed workers. The RRs and information for exposure prevalence are very important in calculating the PAF. In most studies on the PAF, the RRs were taken from previous (especially IARC) reports. Thus, the exposure prevalence is critically influential to the PAF.

In Korea, the officially reported information for occupational carcinogens is limited to manufacturing and mining workers who should have received workers' medical monitoring; this represents neither the total number of workers, nor the general population.

In our analysis, we estimated the exposure prevalence to represent the total population by applying several correction factors, adopting the procedure described in other reports [25] for the first time to Korea.

Our results showed that 1.1% of cancer cases and 1.7% of cancer deaths were attributed to occupation in the 2005 Korean population. The PAF reported by the United States of America [2] and the United Kingdom [29,30] were 4.2% and 2.0% to 4.9%, respectively. In the Nordic countries [4] and France [25], the PAFs were reported at 3.0% and 2.4%, respectively. The results from our study seem to be lower than estimates from other developed countries. The lower PAF for Korea might be appropriate given that 12 kinds of IARC-listed Group 1 carcinogens could not be included in this study because information about the exposed populations was lacking.

On the basis of data from compensation-related cases

investigated by OSHRI for KOSHA, we selected 9 kinds of carcinogens to analyze in this study. Previously, Kang et al. [6] reviewed OSHRI-investigated occupational cancer from the 1990s, showing annual counts of occupational cancer caused by 10 kinds of carcinogens from 1992 to 2000. The major occupational carcinogens selected in our study were similar to those used by Kang et al. [6].

However, the cases investigated by OSHRI for KOSHA were conducted only on those cases requested by KOMWEL. Thus, the compensated occupational cancers for which KOMWEL did not request epidemiologic investigation from OSHRI for KOSHA could not be reviewed when selecting the target carcinogens in our study. We were also unable to review the occupational cancer cases that were compensated through related lawsuits in the court.

In an effort to estimate the global attributed fraction of occupational cancer, regional PAFs were calculated by economically identical sectors from a project led by the World Health Organization (WHO) [3]. In that article, the region known as "Western Pacific B," which included Korea, showed 10% of the PAF for lung cancers and 2% of the PAF for leukemia. In our study, the PAF was relatively lower for lung cancers (7%) and relatively higher for leukemia (4.5%) than the regional values reported by the WHO.

The process of calculating exposure prevalence and the correction factors for each step were adopted from the IARC report on attributable causes of cancers in France [25]. Although the correction factors may be arbitrary instead of evidence based, this process duly reflects lifetime exposure using the limited information about occupational cancer in Korean society. By these means, we were able to calculate the overall PAF of occupational cancer and apply it to the entire economically active population, including workers in every industry and unemployed workers, to arrive at an estimate of lifetime exposure. Although it has many limitations regarding overestimation and underestimation because of the lack of official records regarding these factors, we tried to calculate the national level of the exposure prevalence for 9 kinds of carcinogens using the same method IARC used in its report. Among the 11 carcinogens that could not be included in this study, coal tar pitch might be regarded as the main PAH to which the Korean population has been exposed.

Our results might have underestimated the burden of occupational cancer for several reasons. First, the occupational cancers from primary industries, such as agriculture, forestry and fisheries, the public sector, the military service, and private schools, were not considered as important occupational exposure in this study because of a lack of information.

Second, several important exposure sources were omitted because the study relied on information available at the time. For example, although lung cancer was the main form of occupational cancer and the most prevalent cause was asbestos, asbestos exposure in the construction and ship building sectors was neglected. Third, the long latency period of asbestos-related cancers could have led to an underestimation of the burden, even though we adjusted for the retired workforce by applying correction factors. Fourth, the latency period varies by cancer type. The latency of a non-solid hematopoietic cancer such as leukemia may be shorter than 10 years. From this standpoint, the PAF of leukemia in 2005 should consider the exposure prevalence of 2000. Because we assume 10 years of latency for all 8 kinds of cancers, our estimation may be inaccurate. Finally, the exposure prevalence in this study was calculated from several sources of data, including a national survey of workers in the mining and manufacturing industries from KSIS [12] and specific studies on each carcinogen. For most carcinogens, the number of workers exposed was calculated based on information from 1995; however, the number of workers exposed to cadmium, chromium, and nickel was calculated based on data from 2000. Therefore, the prevalence of exposure to these chemicals might be underestimated.

Overestimation is also possible. Wood dust also could not be specifically identified as hard wood, which is carcinogenic, or soft wood. Another reason for overestimation is that the IARC RRs were not appropriate for Korean society, which is at a different stage of industrialization. The IARC RRs were largely derived from studies conducted in the past, when the exposure rates were generally very high.

The proportion of the population exposed to ionizing radiation was estimated by multiplying the number of industries using radioisotopes (from statistics of the Korea Radioisotope Association [27]) with the average number of workers without applying the correction factor. Thus, the exposed population could be either overestimated or underestimated.

In Korea, industrialization started in the 1960s, and the industries using chemicals greatly expanded and operated actively during the 1970s. During these years, the benzene exposure level might have been 5 to 10 times higher than the exposure limits [31]. However, since the 1980s, the working environment has improved, with several laws enacted for occupational safety and health, and most of the important carcinogens are now controlled by exposure limit. From 1980 onward, exposure to carcinogens decreased to a level lower than that associated with the past of other developed countries. Therefore, the PAFs calculated using IARC RRs may be overestimated.

Because industrialization in Korea is relatively recent, the latency period for some carcinogen exposure-related cancers has not yet expired. Thus, the PAF in this study may be lower than those that will be determined in the future after sufficient latency has occurred.

In this study, we compared the IARC RR-based PAFs and Korean RR-based PAFs of lung cancer, leukemia, and non-Hodgkin's lymphoma. The results showed that Korean RR-based PAFs were lower than IARC RR-based ones. For example, the PAF of lung cancer calculated using IARC RRs was 7.0%; on the contrary, the PAF calculated using Korean RRs was 3.7%.

Despite the possibility of underestimation or overestimation, ours is the first attempt to estimate the occupational cancer burden in the Korean population with the exposure prevalence representing the total population. We tried to achieve a fair estimation of the carcinogen-exposed population from reviewing official records along with research articles. For a more precise estimation of occupational cancer burden, a more accurate survey of the numbers of carcinogen-exposed workers and research on the RR of each carcinogen will be needed.

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