

Lung cancer risk in professional drivers in Korea: A population-based proportionate cancer incidence ratio study

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Abstract: Lung cancer risk in professional drivers in Korea: A population-based proportionate cancer incidence ratio study: Dong-Hee Koh, *et al.* Department of Occupational and Environmental Medicine, International St. Mary's Hospital, Catholic Kwandong University, Republic of Korea—**Objectives:** Professional drivers are exposed to diesel engine exhaust and outdoor air pollution while driving. Diesel engine exhaust and outdoor air pollution are known carcinogens causing lung cancer. However, previous epidemiological studies examining lung cancer risk in professional drivers have not shown a consistent association. In the present study, we evaluated lung cancer risk among Korean professional drivers. **Methods:** Subjects consisted of male drivers aged 30–59 registered in the Korea Central Cancer Registry for lung cancer between 1999 and 2011. Proportionate cancer incidence ratios (PCIRs) for lung cancer were calculated and indirectly age standardized with the male general population. Additional PCIRs were calculated by indirectly adjusting for the effect of cigarette smoking. **Results:** The PCIR for lung cancer in professional drivers during the study period increased significantly (1.20, 95% CI: 1.13–1.26). The increased risk was generally consistent throughout study years and age categories. Adjusting for the effect of cigarette smoking did not change the significance of the associations (1.09, 95% CI: 1.03–1.15). **Conclusions:** Our findings support an association between lung cancer and driver jobs in the Korean male population. However, the association should be further evaluated in a study with a longitudinal design and a quantitative exposure assessment.

(J Occup Health 2015; 57: 324–330)

Received Sept 29, 2014; Accepted Mar 10, 2015

Published online in J-STAGE Apr 17, 2014

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Key words: Cancer, Diesel engine exhaust, Diesel exhaust particle, Driver, Lung cancer, Outdoor air pollution

Diesel engine exhaust and outdoor air pollution were recently classified as human carcinogens causing lung cancer by the International Agency for Research on Cancer (IARC)^{1,2}. Professional drivers are potentially exposed to outdoor air pollution including diesel engine exhaust while working. Many studies have evaluated drivers' occupation-related exposures. Regarding lead exposure, drivers of cars showed higher blood lead levels (31–33 $\mu\text{g/dl}$)³ than the general population when leaded gasoline was used as a motor vehicle fuel. One of the important carcinogenic components of diesel engine exhaust appears to be polycyclic aromatic hydrocarbon (PAH), which are a known carcinogen causing lung cancer. Drivers are reported to be more highly exposed to PAHs than nondrivers⁴. Elemental carbon, organic carbon, and black carbon are major surrogates of diesel engine exhaust⁵. Some studies have shown that drivers are exposed to higher levels of elemental carbon and organic carbon than normal control groups⁶.

Several studies have examined lung cancer risk in professional drivers. A recent meta-analysis that pooled cohort studies and case-control studies showed a significantly increased lung cancer risk⁷. However, studies have shown inconsistent results, and some positive studies also have had limited explanatory power due to a small number of cases or a failure to adjust for important confounders such as smoking^{8,9}. A study analysing census-based estimates of occupational cancer risk in five Nordic countries showed increased standardized incidence ratios (SIRs) for lung cancer in male (1.28, 95% CI: 1.26–1.31) and female (1.46, 95% CI: 1.27–1.67) drivers¹⁰. These previous studies were performed in Western populations,

and few published studies have examined cancer risk in professional drivers in Asian populations. In the present study, we examined the proportionate cancer incidence ratios (PCIR) for lung in Korean professional drivers using a national population-based cancer registry database.

Methods

Study subjects and the KCCR

The study population included male drivers aged 30–59 who were registered in the Korea Central Cancer Registry (KCCR) between Jan. 1, 1999, and Dec. 31, 2011. The KCCR was initiated as a hospital-based cancer registry in 1980, and was expanded to cover the entire population in 1999. National cancer incidence reports for cancer patients diagnosed since 1999 have been published since 2005.

The KCCR has been estimated to have a greater than 97% completeness in the reporting of cancer incidence¹¹. The KCCR database includes information about age, sex, date of diagnosis, cancer site, histological type and job at the time of cancer diagnosis. The primary cancer diagnosis is classified according to the International Classification of Diseases for Oncology (3rd edition, 2000) and converted to the classification system used by the International Classification of Diseases (10th edition, 1994). The KCCR has also included Surveillance, Epidemiology, and End Results (SEER) summary staging (localized/regional/distant) since 2006. The SEER summary stage is the basic way of categorizing how far a cancer has spread from its origin. It has been used by many cancer registries for staging cancer at diagnosis.

We restricted subjects' ages to between 30 and 59 years old for the analyses, because the latency period from carcinogen exposure to cancer recognition is generally more than 10 years¹². Occupation was recorded in the KCCR when the subjects were diagnosed with cancer at hospitals. Accordingly, after the retirement age of 59 years old, patients may have reported their employment status as unemployed rather than reporting their past jobs. Occupation was generally coded according to the major groupings in the Korea Standard Classification of Occupations (5th edition, 2000). "Driver" was included as one of the job titles in the KCCR occupational classification. Therefore, a driver was defined in this study as a person who was recorded as a driver on his clinical chart and registered as a lung cancer patient in the KCCR.

Statistical analysis

The study of proportionate cancer incidence ratios (PCIRs) uses the same method employed in calculating proportionate mortality ratios (PMRs). PMR

studies are used when the only available information comes from the death certificates of a group of persons with the same occupation¹³. For rare causes of death, a PMR is a reasonable approximation of a standardized mortality ratio (SMR), which is a reasonable approximation of a standardized rate ratio (SRR)¹³.

Lung cancer PCIRs were calculated using the indirectly age-standardized cancer incidence of Korean drivers compared with the general population's cancer incidence. The expected number of lung cancers due to working as a driver was calculated based on the proportion of lung cancer cases to all cancers in the general population¹³. The proportions of lung cancer incidence to the incidence of all cancers in Korean male populations aged between 30 and 59 for each year of the study period (1999–2011) were used as reference proportions. The age groups were categorized in five-year intervals, between 30 and 59 years old. The expected number of cancer cases was calculated by multiplying the number of all cancer cases in drivers by the proportion of lung cancer cases to all cancers in the general male population. After indirect age standardization, the sum of the observed number of cases was divided by the sum of the expected number of cases, which yielded PCIRs. Ninety-five percent confidence intervals were also calculated¹².

Cigarette smoking is a major cause of lung cancer; therefore, we indirectly adjusted for the confounding effects of cigarette smoking using a formula¹⁴. Smoking rates in drivers aged between 30 and 59 (current smokers, 63.4%; ever-smokers, 79.9%), and the male general population aged between 30 and 59 (current smokers, 51.9%; ever-smokers, 81.3%) were obtained from the Third Korean Working Conditions Survey (KWCS, 2011) and the Korea National Health and Nutrition Examination Survey (KNHANES, 2011), respectively. The relative risk (RR) of lung cancer for current smokers versus current nonsmokers was established to be 2.58 from the literature¹⁵. The current smoking rates of drivers and the male general population, and the RR of lung cancer among current smokers, were used to indirectly adjust for the cigarette smoking effect¹⁴. All analyses were performed using SAS 9.2 (SAS Institute, Inc. Carry, NC, USA).

Ethical approval

This study protocol was reviewed and approved by the Institutional Review Board of the National Cancer Center, Republic of Korea.

Results

Between 1999 and 2011, 1,280 drivers (11.1%) of the 11,572 male drivers registered in the KCCR were diagnosed with lung cancer, while 33,924 men (9.0%) of the 378,440 men registered in the KCCR

Table 1. Characteristics of male drivers with lung cancer and the general male population of lung cancer patients

Variables	Drivers		General population		<i>p</i> value*	
	Cases	%	Cases	%		
Total	1,280	100.0	33,924	100.0		
Incidence year	1999–2002	288	22.5	9,717	28.6	<0.001
	2003–2005	272	21.3	7,508	22.1	
	2006–2008	309	24.1	8,025	23.7	
	2009–2011	411	32.1	8,674	25.6	
Age group	30–39	40	3.1	1,450	4.3	0.0095
	40–49	329	25.7	7,701	22.7	
	50–59	911	71.2	24,773	73.0	
Histology	Squamous cell carcinoma	358	28.0	10,044	29.6	<0.001
	Adenocarcinoma	534	41.7	12,379	36.5	
	Small-cell carcinoma	189	14.8	4,567	13.5	
	Large-cell carcinoma	53	4.1	1,232	3.6	
	Others	146	11.4	5,702	16.8	
SEER summary stage (Since 2006, n=720)	Localized	111	15.4	3,007	18.0	0.1276
	Regional	219	30.4	4,648	27.8	
	Distant	322	44.7	7,242	43.4	
	Unknown	68	9.4	1,802	10.8	

**p* values were calculated using chi-square tests for categorical variables. SEER, Surveillance, Epidemiology, and End Results.

were diagnosed with lung cancer. The year categories with the highest incidence were 2009–2011 for drivers (32.1%) and 1999–2002 for the male general population (28.6%). The most common age group was 50–59 years, both for drivers (71.2%) and the male general population (73%). The most frequently reported histological type was adenocarcinoma both for drivers (41.7%) and male persons in the general population (36.5%). The most common SEER summary stage was “distant” both for drivers (44.7%) and male persons in the general population (43.4%). The distributions of incidence year, age group, and histological type showed statistically significant differences between drivers and the general population, according to chi-square tests (Table 1).

Professional drivers showed a significantly elevated PCIR for lung cancer (1.20, 95% CI: 1.13–1.26), and the elevated PCIR remained significant after adjusting for the effect of cigarette smoking (1.09, 95% CI: 1.03–1.15). Unadjusted PCIRs were significantly elevated across incidence year categories, while the smoking-adjusted PCIR was significantly elevated in the 2009–2011 category (1.13, 95% CI: 1.02–1.24). For age group, unadjusted PCIRs were significantly elevated across all age groups, while the smoking-adjusted PCIR was significantly elevated only in the 40–49 group (1.26, 95% CI: 1.12–1.39). For histological type, unadjusted PCIRs for squamous cell carcinoma (1.21, 95% CI: 1.09–1.34) and adenocar-

cinoma (1.30, 95% CI: 1.19–1.41) were significantly elevated, while the smoking-adjusted PCIR was significantly increased only in adenocarcinoma (1.18, 95% CI: 1.08–1.29). For SEER summary stages, unadjusted PCIRs were elevated in regional, distant, and unknown categories, while smoking-adjusted PCIRs were elevated only in regional and unknown categories (Table 2).

Discussion

In the present study, the smoking-adjusted PCIR for lung cancer was significantly elevated in Korean male drivers; these findings are consistent with those of previous meta-analytical studies. Tsoi and Tse⁷⁾ reported a significantly increased risk of lung cancer (pooled smoking-adjusted RR 1.18, 95% CI: 1.05–1.33) in professional drivers. Bhatia *et al.*⁸⁾ reported a pooled RR of 1.33 (95% CI: 1.24–1.44), and Lipsett and Campleman⁹⁾ reported a pooled smoking-adjusted RR of 1.47 (95% CI: 1.29–1.67).

A study pooling case-control studies in Europe and Canada reported an increased odds ratio (OR) of 1.31 (95% CI: 1.19–1.43) in the highest quartile of cumulative diesel exposure versus unexposed populations¹⁶⁾. In addition, a study combining 17 European cohorts to examine the association between air pollution and lung cancer showed a statistically significant association between lung cancer and PM₁₀ (particulate matters less than 10 μm in diameter) (hazard ratio [HR]

Table 2. Proportionate cancer incidence ratios (PCIRs) for lung cancer in male drivers

Variables		Unadjusted PCIR (95% CI)	Smoking-adjusted PCIR (95% CI)
Total		1.20 (1.13–1.26)	1.09 (1.03–1.15)
Incidence year	2003–2005	1.25 (1.10–1.39)	1.13 (1.00–1.27) *
	2006–2008	1.19 (1.05–1.32)	1.08 (0.96–1.20)
	2009–2011	1.24 (1.12–1.36)	1.13 (1.02–1.24)
Age group	30–39	1.48 (1.02–1.94)	1.34 (0.93–1.76)
	40–49	1.38 (1.23–1.53)	1.26 (1.12–1.39)
	50–59	1.13 (1.06–1.20)	1.03 (0.96–1.10)
Histology	Squamous cell carcinoma	1.21 (1.09–1.34)	1.10 (0.99–1.22)
	Adenocarcinoma	1.30 (1.19–1.41)	1.18 (1.08–1.29)
	Small-cell carcinoma	1.03 (0.88–1.17)	0.93 (0.80–1.07)
	Large-cell carcinoma	1.37 (1.00–1.73) *	1.24 (0.91–1.56)
	Others	0.87 (0.73–1.01)	0.79 (0.66–0.92)
SEER summary stage (Since 2006, n=720)	Localized	1.05 (0.87–1.23)	0.96 (0.79–1.12)
	Regional	1.27 (1.11–1.43)	1.15 (1.01–1.30)
	Distant	1.18 (1.06–1.30)	1.07 (0.96–1.18)
	Unknown	1.24 (1.14–1.34)	1.13 (1.03–1.22)

* 95% confidence intervals include 1. SEER, Surveillance, Epidemiology, and End Results.

1.22, 95% CI: 1.03–1.45 per $10 \mu\text{g}/\text{m}^3$) and $\text{PM}_{2.5}$ (particulate matters less than $5 \mu\text{m}$ in diameter) (HR 1.18, 95% CI: 0.96–1.46 per $5 \mu\text{g}/\text{m}^3$)¹⁷). Our findings may support the association between diesel engine exhaust or outdoor air pollution and lung cancer.

Although the IARC has classified diesel engine exhaust as a definite human carcinogen, the debate over the carcinogenicity of diesel engine exhaust is still ongoing. One of the main reasons may be the lack of a clear exposure-response relationship. Gamble *et al.*¹⁸) and Sun *et al.*¹⁹) reviewed the literature and concluded that there was no strong, consistent evidence of an exposure-response relationship between diesel engine exhaust exposure and lung cancer. On the other hand, in a meta-analysis, Vermeulen *et al.*²⁰) studied the exposure-response relationship from three critical studies using elemental carbon as an exposure surrogate and found a significant dose-related effect for lung cancer mortality. They concluded that 6% of annual lung cancer deaths are attributable to diesel engine exhaust exposure²⁰), while Hoek and Raaschou-Nielson estimated the population attributable fraction (PAF) of lung cancer mortality due to air pollution exposure in the entire population to be 3–29%²¹). The ongoing uncertainty about the exposure-response relationship may be partially due to the difficulty in measuring diesel engine exhaust. Diesel engine exhaust is a complex mixture of hundreds of constituents in gas or particulates, including carcinogenic PAHs²²). The quantity of these constituents is depen-

dent on many factors, such as fuel type and operating conditions. In previous studies, job title, work duration, PM_{10} , $\text{PM}_{2.5}$, PM_1 (particulate matters less than $1 \mu\text{m}$ in diameter), black carbon, organic carbon, and elemental carbon have been used as exposure surrogates^{18, 19}), which illustrates the challenge of measuring diesel engine exhaust exposure. Most of the elemental carbon emitted from mobile sources originates from diesel exhaust sources, with smaller percentages from gasoline engine exhaust²³).

To our knowledge, our study is the first to evaluate PCIRs for lung cancer in professional drivers using a nationwide cancer registry database. The major strength of our study lies in the large number of lung cancer cases, as previous cohort and case-control studies have had limited study power due to a small number of cases. In addition, the associations in the current study were generally consistent across time periods and age categories, which may provide additional confidence in the true associations.

In the present study, we have not accounted for temporal changes in diesel engine exhaust exposure. Previous diesel engine exhaust exposure assessments used PM_{10} ²⁴), NO_2 ²⁴), coefficient of haze (COH)²⁵) or CO ²⁶) as surrogates for estimating temporal trends in diesel engine exhaust or air pollutant exposure. Since the 1990s, relevant environmental regulations have been enforced; by adopting “clean diesel technology” (Euro 6), the amount of exhaust particulates was reduced by up to 99%²⁷). Although new diesel

technologies have been developed, the number of diesel-powered vehicles has increased from the 1990s through to the 2010s in Korea, and air quality therefore was not substantially improved^{28, 29}. Thus, the temporal trends in diesel engine exhaust would have limited effects on our findings, considering the latency period of more than 10 years. In addition, the lack of measurement data made it difficult to estimate diesel engine exhaust exposure in the 1970s and 1980s, during which exposure may have had a substantial effect on lung cancer development, considering latency periods.

Diesel engine exhaust exposure in drivers is known to be correlated with vehicle age, because leaks from the vehicle's rubber seals allow exhaust from the engine to enter the vehicle³⁰. Job type, ventilation, window status, cigarette smoking (both direct and indirect), and workplace characteristics may also be associated with personal exposure. Regarding background exposure, relative humidity, wind speed, adjacent industrial facility, and area are associated with diesel engine exhaust exposure³¹. In addition, old vehicles generate more black carbon than new ones³². Our study is an ecological study with an inherent inability to account for individual-level factors, which is an important limitation.

Cigarette smoking is one of the major causes of lung cancer, as well as a source of particulates similar to diesel engine exhaust. For instance, Davis *et al.*³⁰ reported that smokers in the trucking industry showed higher elemental carbon, organic carbon, and PM_{2.5} exposure than nonsmoking workers. Because we could not obtain the study subjects' smoking histories, we indirectly adjusted for the effect of smoking. In the smoking adjustment formula¹⁴, age is not further adjusted, which may lead to a potential bias if two population structures are substantially different. Although the adjustment did not change the significance of the associations, our findings should be interpreted cautiously due to the inherent limitations of the ecological approach; a longitudinal study adjusting for cigarette smoking needs to be performed to elucidate the causal relationship.

With regard to the histological subtypes of lung cancer, our study showed that the PCIR for lung squamous cell carcinoma was marginally elevated in Korean drivers. A previous study by Boffetta *et al.*³³ also showed a dose-response relationship between diesel engine exhaust exposure and the risk of lung squamous cell carcinoma. However, the association between diesel engine exhaust exposure and squamous cell carcinoma may be overestimated due to a residual confounding or interaction effect with cigarette smoking. Our study also showed that the risk of adenocarcinoma was increased in drivers compared with

the general population. Indeed, animal experimental studies have also reported that adenocarcinoma was the dominant lung carcinoma after rats or mice were exposed to diesel gas or carbon black³⁴. In addition, HRs for PM_{2.5} and PM₁₀ exposures were significantly associated with adenocarcinoma alone, among the histological subtypes of lung cancer¹⁷. However, we could not draw any conclusions regarding the histological subtypes in this study, because the associations between diesel engine exhaust exposure and the risk of specific histological subtypes of lung cancer were inconsistent and heterogeneous¹⁸.

The risk of lung cancer may differ according to the type of professional driver job and area. Taxi drivers have shown a higher lung cancer risk than bus drivers³⁵, and professional drivers in rural areas have shown no significant increase in lung cancer risk³⁶. In the present study, we could not account for these factors because data were not available on the type of driver job, type of vehicle and area (county/district level). This is a limitation of our study. In addition, we did not consider female drivers, as the number was small. Robinson *et al.*³⁷ showed a significantly increased PMR for lung cancer in female drivers after adjusting for the effect of smoking.

There may have been job misclassifications in our study. In the KCCR database, the current job at the time of diagnosis is recorded as the patient's job. For instance, if a lifetime driver changes jobs just before his cancer diagnosis, this new job would be recorded. The opposite situation may also have occurred. Indeed, we suspect the opposite situation would be more common. A lot of people in Korea have a driver's license, and it is relatively easy for the general population to change jobs and become a driver. Another potential source of misclassification is that the driver job category may include other transportation-related jobs. For instance, railway signal and switch operators who may not be directly exposed to diesel engine exhaust may be classified as drivers. Despite potential misclassifications, the high specificity of job or exposure-type might result in a real exposure-response relationship. In Korea, there has been no official document or study classifying the occupations or job types of cancer patients. This may hamper research examining the risks associated with various occupations or jobs. The job information collection system in the KCCR needs to be further developed to include information on employment history and the type of car driven, which could then be used to evaluate lung cancer among professional drivers. This information would help to assess drivers' levels of exposure to diesel engine exhaust and other vehicle pollutants.

In the present study, we used the PCIR method to

examine the association between driver job and lung cancer risk. The PCIR method is often criticized for potential biases¹²⁾. For instance, it will be biased upward when the all-cancer SIR is low (vice versa)³⁸⁾. This method would be useful to investigate a novel exposure and disease relationship rather than well-known associations. Therefore, our results should be interpreted cautiously.

There were no significant differences in SEER summary stages between drivers and the general population, which suggests there was no early detection effect in any group.

Besides diesel engine exhaust, drivers are also exposed to vibration, musculoskeletal strain, and traffic jams and are prone to irregular meal times, inactivity, obesity and isolation due to irregular work schedules. Fine particulate air pollution is regarded as a risk factor for cardiovascular disease, and working for years in the trucking industry with tasks such as a long haul driving is associated with higher ischemic heart disease mortality than in the general population of drivers²²⁾. Other studies have reported an increased risk of aggressive prostate cancer³⁹⁾ and facial skin cancer⁴⁰⁾. Exposure assessment efforts may be a necessary first step to protect workers from work-related adverse health effects, as drivers are a high-risk group for diesel engine exhaust exposure.

In summary, professional drivers showed an elevated risk of lung cancer in our study. Attention should be paid to the health of professional drivers to prevent lung cancer related to diesel engine exhaust exposure.

Acknowledgments: This study was supported by a National Cancer Center Grant (NCC-1310220).

Conflict of interests: The authors declare that they have no conflicts of interest.

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