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Occupational exposures and risk of esophageal and gastric cardia cancers among male Swedish construction workers

Catarina Jansson[1,*], Anna L.V. Johansson[1], Ingvar A. Bergdahl[2], Paul W. Dickman[1], Nils Plato[3]
Johanna Adami[4], Paolo Boffetta[1,5], & Jesper Lagergren[1,6]
[1]*Department of Medical Epidemiology and Biostatistics, Karolinska Institutet, 281SE-171 77, Stockholm, Sweden;* [2]*Occupational Medicine, Department of Clinical Medicine and Public Health, Umeå University, Umeå, Sweden;* [3]*Division of Occupational Health, Department of Public Health Sciences, Karolinska Institutet, Stockholm, Sweden;* [4]*Clinical Epidemiology Unit, Department of Medicine, Karolinska University Hospital, Stockholm, Sweden;* [5]*International Agency for Research on Cancer, Lyon, France;* [6]*Department of Surgical Sciences, Karolinska Institutet, Stockholm, Sweden*

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Abstract

Objective: The rising incidence and the strong male predominance among patients with esophageal and gastric cardia adenocarcinoma remain unexplained. We hypothesized that occupational airborne exposures in a traditional male dominated industry might contribute to these observations.
Methods: A prospective, large cohort study of Swedish construction workers was linked to the Swedish population-based registers of Cancer, Causes of Death and Total Population. 260,052 men were followed from 1971 through 2000. Industrial hygienists assessed specific exposures for 200 job titles, and occupational airborne exposures were analyzed separately and combined. Incidence rate ratios (IRR), with 95% confidence intervals (CI), were estimated in multivariable Cox regression models adjusted for attained age, calendar period, smoking status and body mass.
Results: We found positive associations between high exposure to asbestos (IRR 4.5 [95% CI 1.4–14.3]) and cement dust (IRR 3.8 [95% CI 1.5–9.6]) and risk of esophageal adenocarcinoma. Associations were seen between high exposure to asphalt fumes (IRR 2.3 [95% CI 1.0–5.3]) and wood dust (IRR 4.8 [95% CI 1.2–19.4]) and risk of cardia adenocarcinoma. No consistent associations regarding esophageal squamous-cell carcinoma were found.
Conclusions: Exposure to asbestos and cement dust may be risk factors for esophageal adenocarcinoma, and exposure to asphalt fumes and wood dust may increase the risk of cardia adenocarcinoma. However, these associations cannot explain the major sex differences or the increasing incidence trends of these tumors.

Introduction

The reasons for the rising incidence of esophageal and gastric cardia adenocarcinoma reported in several European countries and in the United States remain unexplained [1–4]. Gastroesophageal reflux [5–7], high body mass index (BMI) [8, 9], and male sex (male/female ratio 7:1) [2, 10] are the strongest known risk factors, but the distribution of these exposures over time do not follow the adenocarcinoma occurrence completely. The sudden and rapid increase of adenocarcinoma of the esophagus [11] suggests that environmental exposures, introduced before the rise began in the 1970s, and mainly occurring among men, might play an important part in explaining the increasing incidence [12, 13]. An explanation that could fit with these observations is that certain occupational risk exposures only exist in male dominated occupations and industries. Studies of the influence of occupational exposures in the etiology of adenocarcinoma of the esophagus or the gastric cardia are rare. Only one prior study dealing with occupations

* Address correspondence to: Catarina Jansson, Department of Medical Epidemiology and Biostatistics, Karolinska Institutet, P.O. Box 281, SE-171 77, Stockholm, Sweden. Fax: +46-8-314975; E-mail: catarina.jansson@meb.ki.se

and esophageal and cardia cancers has studied these tumors as separate diseases [14]. Here occupational groups, and not specific exposures, were examined, however. The majority of previous studies of occupational exposures and risk of esophageal cancer have focused on squamous-cell carcinoma of the esophagus, a cancer type where the incidence rate has remained stable or declined during the last 20 years [2, 15]. There is also a male predominance three to one among patients with esophageal squamous-cell carcinoma, but this sex difference is entirely explained by sex differences in the exposure to the dominating risk factors for this cancer, i.e. tobacco and alcohol use [16, 17]. These risk exposures have been estimated to be responsible for 90% of all cases of squamous-cell carcinoma of the esophagus in Western populations [18].

The aim of our study was to investigate occupational airborne exposures among men in relation to risk of esophageal and cardia cancers, in particular adenocarcinomas. We hypothesized that certain occupational exposures in the construction industry, e.g. asbestos, fumes, dust, fibers and solvents, could be deposited in the airway region, and then inhaled or swallowed and thereby directly act on the mucosa of the esophagus or the gastric cardia. To be able to achieve our aim, we used prospective data from a large cohort of Swedish construction workers [19].

Materials and methods

The cohort

The Swedish Construction Workers Cohort consists of nearly 400,000 Swedish construction workers and other employees within the construction industry. All of these employees were between 1971 and 1993 regularly invited to health examinations by a nationwide occupational health service organization ('Bygghälsan'). On average three health examinations per registered individual were conducted. Information on job titles and other exposures was collected through self-administered questionnaires as well as forms completed by the staff of the health organization. The vast majority (95%) of the cohort members were males. Due to the small number of women in the cohort, and the low incidence of esophageal and cardia cancers among women, we restricted the study to men.

Register linkages and cancer diagnoses

The National Registration Number (NRN), a unique ten-digit number assigned to all residents in Sweden, identified each individual cohort member. To identify all cases of esophageal or cardia cancer occurring within the cohort the NRN's were used for linkage to the nationwide Swedish Cancer Register. This register has coded esophageal cancers since 1958, and the specific site gastric cardia cancer since 1969, according to the 7th Revision of the International Classification of Diseases (ICD-7). The completeness of the Cancer Register has been found to be 98% [20]. The ICD-7 four-digit code for esophageal cancer is 1500, and for gastric cardia cancer 1511. The ICD-7 three-digit histopathological code for adenocarcinoma is 096, and for squamous-cell carcinoma 146. For correct censoring of persons not at risk for esophageal or cardia cancer in the cohort and for complete follow-up, the cohort members were linked to the nationwide Swedish registers of Causes of Death, to ascertain date of death, and the Total Population, to identify men who had emigrated.

Exposure assessment

The exposure assessment was based on job titles and has been employed in previous studies [21, 22]. Only the job title at each worker's first health examination was used, since the information available was insufficient for constructing lifetime occupational histories. Between 1971 and 1976 a survey was carried out by the occupational health service organization, where the exposure pattern within each occupation was studied at visits to approximately five different work sites in different geographical regions in Sweden [21, 22]. The main job tasks for over 200 job title categories existing in the Swedish construction industry were selected, and environmental descriptions were made by industrial hygienists. Assessments were made for 212 job titles used to describe each individual's occupation during the period 1971–1985/86. After 1985, only 90 job titles were used. Based on the original job-exposure matrix, a similar matrix for these 90 job titles was developed by an experienced industrial hygienist (I.A.B.). Twelve agents were included in the matrix; asbestos, asphalt fumes, cement dust, concrete dust, diesel exhaust, epoxy resins, isocyanates, man-made mineral fibers, metal fumes, organic solvents, quartz dust, and wood dust. Each of these exposures was graded on an ordinal scale from zero to five, where level three corresponded to the Swedish threshold limit value (TLV) at the time of the study. We added an exposure level of 0.5 for diesel exhaust, including e.g. car drivers, who were considered as unexposed in the original job exposure matrix. We categorized the exposure level scales into no exposure (0), moderate exposure (0.5–1) and high exposure (2–5). For the majority of the 12 agents most workers were classified as one within the moderate exposure category, and

most workers were classified as two or three within the high exposure category. We also examined combined exposure to dust and fumes. Dust exposure was defined as exposure to either of asbestos, cement dust, concrete dust, mineral fibers, quartz dust or wood dust. Similarly, fume exposure was defined as exposure to either of diesel exhaust, asphalt fumes or metal fumes.

Exclusions of cohort members

The cohort included 389,717 members. From these we excluded 19,478 women, 3 men with a diagnosis of an esophageal or gastric cardia cancer event before their first health examination, 43 men with an unspecified or other histological type of esophageal or gastric cardia cancer, 12 men with incorrect death dates, and 38,204 men with insufficient or missing information on job title. Furthermore, 71,925 men were excluded due to missing information regarding smoking status or BMI. After these exclusions we ended up with a total of 260,052 male individuals included in the final statistical analyses.

Statistical analyses

The cohort members were followed from the date of their first health examination through December 31, 2000, date of death, date of emigration, or date of a primary esophageal adenocarcinoma, gastric cardia adenocarcinoma or esophageal squamous-cell carcinoma diagnosis, whichever came first. The three different cancer diagnoses were assumed to be independent events, i.e. men diagnosed with one of the three tumor types of interest were still considered to be at risk for the other two. We estimated incidence rate ratios (IRR) and 95% confidence intervals (CI) by Cox regression analysis [23], using calendar time as the underlying time scale. Models were estimated using the PHREG procedure in SAS [24]. In multivariable models, adjustments were made for attained age (classified into five-year age groups), calendar period at entry into the cohort (in three categories; 1971 to 1975, 1976 to 1980 and 1981 to 1993), tobacco smoking status at entry into the cohort (in three categories; never, previous and current) and BMI (kg/m^2) at entry into the cohort (in four categories; ≤21.9 underweight, 22.0–24.9 normal, 25.0–29.9 overweight and ≥30.0 obese). Observations with missing data on any covariate included in the models were Zexcluded from the analyses. Information regarding smoking status was not recorded in the cohort between 1975 and 1978, which means that all men with a first health examination during these years were excluded from the multivariable models. The overall effect of each covariate was assessed by a Wald test of homogeneity across all exposure strata. This test considers all strata, rather than just pair wise comparison to the reference group.

The study was approved by the Ethics Committee at Umeå University (Umeå, Sweden).

Results

Study participants

The total of 260,052 male study participants together contributed with over five million person-years at risk of esophageal or gastric cardia cancer during follow-up of the cohort (Table 1). We identified 64 patients with esophageal adenocarcinoma, 165 patients with gastric cardia adenocarcinoma and 179 patients with esophageal squamous-cell carcinoma. Some characteristics of these patients are presented in Table 1. The total incidence rate per 100,000 person-years was 1.3 for esophageal adenocarcinoma, 3.3 for gastric cardia adenocarcinoma and 3.6 for esophageal squamous-cell carcinoma. The incidence rates were higher for all esophageal and cardia cancer patients with a first examination during the period 1970 through 1975, and for those who were current smokers or had a BMI above 30 at entry into the cohort (Table 1).

Occupational exposures

Distribution of occupational airborne exposures

The prevalence of each of the 12 occupational exposures included in the study is presented in Table 2. Among all study participants as many as 56% were exposed to dust (the combined dust variable), while 22% were exposed to fumes (the combined fumes variable). The occurrence of dust exposure among the patients with esophageal adenocarcinoma, cardia adenocarcinoma and esophageal squamous-cell carcinoma were 64, 63 and 65%, respectively, and the corresponding percentages exposed to fumes among the three groups were 34, 23 and 26, respectively (Table 2).

Esophageal adenocarcinoma

We found positive seemingly dose–response associations between exposure to both asbestos and cement dust and the risk of esophageal adenocarcinoma (Table 2). Among men with high asbestos exposure a more than 4-fold significantly increased risk was found (IRR 4.5 [95% CI 1.4–14.3]) (Table 2), and among workers with high exposure to cement dust we found an almost fourfold significantly increased risk of this tumor (IRR 3.8 [95% CI 1.5–9.6]) (Table 2). The point estimate for

Table 1. No. of participants, person-years and incidence rates (IR)[a] for esophageal or gastric cardia cancers by attained age, calendar period, tobacco smoking status and body mass index

Characteristic	No. of Subjects[b] n(%)	Person-years[c]	Adenocarcinoma of esophagus		Adenocarcinoma of gastric cardia		Squamous-cell carcinoma of esophagus	
			All cases	IR[a]	All cases	IR[a]	All cases	IR[a]
Attained age								
≤34	156,682	1,456,620	1	0.1	0	0	0	0.0
35–39	145,343	588,505	0	0	1	0.2	0	0.0
40–44	133,235	555,291	2	0.4	2	0.4	1	0.2
45–49	126,907	534,953	6	1.1	4	0.7	4	0.7
50–54	120,499	488,374	6	1.2	11	2.3	14	2.9
55–59	104,147	409,628	14	3.4	16	3.9	24	5.9
60–64	85,476	349,036	5	1.4	31	8.9	35	10.0
65–69	65,222	276,889	5	1.8	42	15.2	33	11.9
70–74	46,691	190,526	9	4.7	33	17.3	34	17.8
75–79	29,896	111,816	8	7.2	18	16.1	20	17.8
80–84	15,166	48,421	6	12.4	7	14.5	8	16.5
≥85	5281	14,415	2	13.9	0	0	6	41.6
Calendar period at entry into the cohort								
1971–1975	122,443 (47)	3,017,792	52	1.7	141	4.7	147	4.9
1976–1980	24,482 (9)	501,036	5	1.0	12	2.4	13	2.6
1981–1993	113,127 (44)	1,505,651	7	0.5	12	0.8	19	1.3
Tobacco smoking status at entry into the cohort								
Never	112,807 (43)	1,988,744	11	0.5	27	1.4	16	0.8
Previous	41,704 (16)	891,294	13	1.4	38	4.3	14	1.6
Current	105,541 (41)	2,214,441	40	1.9	100	4.7	149	7.0
Body mass index[d] *at entry into the cohort*								
≤21.9 underweight	66,894 (26)	1,286,436	7	0.5	22	1.7	43	3.3
22.0–24.9 normal weight	102,247 (39)	1,990,811	24	1.2	61	3.1	77	3.9
25.0–29.9 overweight	78,936 (30)	1,530,250	27	1.8	68	4.4	50	3.3
≥30.0 obese	11,975 (5)	216,982	6	2.7	14	6.4	9	4.1
Total[e]	260,052	5,024,479	64	1.3	165	3.3	179	3.6

[a] Incidence rates per 100,000 person-years.

[b] The reported numbers of subjects for attained age are the numbers for the analyses of esophageal adenocarcinoma. Values are slightly different for the other two outcomes due to the different end-points.

[c] The reported person-years are the numbers for the analyses of esophageal adenocarcinoma. Values are slightly different for the other two outcomes due to the different end-points.

[d] Body mass index calculated as bodyweight in kilograms divided by the square of body height in meters (kg/m^2).

[e] Observations with missing on any charestristic included in this table were excluded from the analyses.

combined fume exposure was 60% increased, but not statistically significant (IRR 1.6 [95% CI 0.9–2.7]) (Table 2). There were no statistically significant associations between any of the other specific occupational exposures included in the study, or the combined dust variable, and risk of esophageal adenocarcinoma (Table 2).

Gastric cardia adenocarcinoma

We found a two-fold significantly increased risk of gastric cardia adenocarcinoma among men with high asphalt fumes exposure, compared to unexposed men (IRR 2.3 [95% CI 1.0–5.3]) (Table 2). Furthermore, evidence of a positive association between wood dust exposure and the risk of this tumor was found, where a significantly increased risk was seen among highly exposed individuals compared to non-exposed (IRR 4.8 [95% CI 1.2–19.4]) (Table 2). We found no other statistically significant associations between the specific occupational exposures, or the combined dust or fume exposure variables, and risk of cardia adenocarcinoma (Table 2).

Esophageal squamous-cell carcinoma

We found evidence of positive associations between moderate cement dust exposure (IRR 1.5 [95% CI 1.0–2.3]), and moderate mineral fibers exposure (IRR 1.7 [95% CI 1.0–3.0]), and the risk of esophageal squamous-cell carcinoma, but no apparent dose–response relations were seen (Table 2). There were no statistically

Table 2. No. of participants, person-years and incidence rate ratios (IRR)[a] for esophageal or gastric cardia CANCERs Associated with occupational exposures among Swedish construction workers

Occupational exposure	No. of subjects	Person-years[b]	Adenocarcinoma of esophagus			Adenocarcinoma of gastric cardia			Squamous-cell carcinoma of esophagus		
	n (%)		All cases	IRR[a] (95% CI)	*p*-value[c]	All cases	IRR[a] (95% CI)	*p*-value	All cases	IRR[a] (95% CI)	*p*-value
Asbestos											
No exposure	249,343 (96)	4,792,980	58	1.0 (reference)		161	1.0 (reference)		170	1.0 (reference)	
Moderate exposure	7137 (3)	153,120	3	1.7 (0.5–5.4)		3	0.6 (0.2–2.0)		8	1.5 (0.7–3.0)	
High exposure	3572 (1)	78,379	3	4.5 (1.4–14.3)	0.03	1	0.6 (0.1–4.2)	0.63	1	0.5 (0.1–3.7)	0.44
Asphalt fumes											
No exposure	255,286 (98)	4,930,026	64	–		159	1.0 (reference)		176	1.0 (reference)	
Moderate exposure	– (–)	–									
High exposure	4766 (2)	94,453	0	–		6	2.3 (1.0–5.3)	0.04	3	1.0 (0.3–3.0)	0.95
Cement dust											
No exposure	237,762 (91)	4,599,170	51	1.0 (reference)		146	1.0 (reference)		146	1.0 (reference)	
Moderate exposure	18,866 (7)	352,068	8	1.6 (0.7–3.3)		15	0.9 (0.5–1.5)		26	1.5 (1.0–2.3)	
High exposure	3424 (1)	73,241	5	3.8 (1.5–9.6)	0.01	4	0.8 (0.3–2.2)	0.82	7	1.5 (0.7–3.3)	0.09
Concrete dust											
No exposure	161,726 (62)	3,112,199	39	1.0 (reference)		100	1.0 (reference)		101	1.0 (reference)	
Moderate exposure	48,936 (19)	905,093	13	1.2 (0.6–2.3)		30	1.0 (0.7–1.6)		33	1.1 (0.7–1.6)	
High exposure	49,390 (19)	1,007,186	12	0.9 (0.5–1.7)	0.73	35	0.9 (0.6–1.3)	0.86	45	1.1 (0.8–1.6)	0.72
Diesel exhaust											
No exposure	226,098 (87)	4,352,122	49	1.0 (reference)		139	1.0 (reference)		149	1.0 (reference)	
Moderate exposure	28,155 (11)	552,993	11	1.4 (0.7–2.8)		19	0.9 (0.6–1.5)		22	1.0 (0.6–1.5)	
High exposure	5799 (2)	119,364	4	2.1 (0.8–5.8)	0.25	7	1.2 (0.5–2.5)	0.85	8	1.3 (0.6–2.6)	0.82
Epoxy resins											
No exposure	257,659 (99)	4,977,733	62	1.0 (reference)		163	1.0 (reference)		175	1.0 (reference)	
Moderate exposure	2393 (1)	46,745	2	2.6 (0.6–10.5)	0.19	2	0.9 (0.2–3.6)	0.86	4	1.6 (0.6–4.3)	0.35
High exposure	–	–									
Isocyanates											
No exposure	243,483 (94)	4,759,549	62	1.0 (reference)		154	1.0 (reference)		173	1.0 (reference)	
Moderate exposure	15,691 (6)	248,954	2	0.8 (0.2–3.3)		10	1.5 (0.8–2.9)		6	0.8 (0.3–1.8)	
High exposure	878 (–)	15,976	0	–	0.95	1	2.3 (0.3–16.7)	0.31	0	–	0.84
Metal fumes											
No exposure	235,391 (91)	4,542,669	56	1.0 (reference)		154	1.0 (reference)		161	1.0 (reference)	
Moderate exposure	1104 (–)	18,268	0	–		1	1.2 (0.2–8.9)		1	1.4 (0.2–9.7)	
High exposure	23,557 (9)	463,541	8	1.5 (0.7–3.3)	0.52	10	0.8 (0.4–1.4)	0.67	17	1.2 (0.7–2.0)	0.77
Mineral fibers											
No exposure	240,425 (92)	4,636,255	57	1.0 (reference)		156	1.0 (reference)		163	1.0 (reference)	
Moderate exposure	12,314 (5)	245,297	4	1.4 (0.5–3.9)		7	0.9 (0.4–1.9)		14	1.7 (1.0–3.0)	
High exposure	7313 (3)	142,926	3	2.3 (0.7–7.2)	0.33	2	0.6 (0.1–2.4)	0.74	2	0.5 (0.1–2.1)	0.10

Table 2. (Continued)

Occupational exposure	No. of subjects	Person-years[b]	Adenocarcinoma of esophagus			Adenocarcinoma of gastric cardia			Squamous-cell carcinoma of esophagus		
	n (%)		All cases	IRR[a] (95% CI)	*p*-value[c]	All cases	IRR[a] (95% CI)	*p*-value	All cases	IRR[a] (95% CI)	*p*-value
Quartz dust											
No exposure	208,262 (80)	3,989,028	46	1.0 (reference)		124	1.0 (reference)		126	1.0 (reference)	
Moderate exposure	42,745 (16)	849,552	15	1.3 (0.7–2.3)		32	1.0 (0.7–1.5)		42	1.3 (0.9–1.8)	
High exposure	9045 (3)	185,899	3	1.0 (0.3–3.2)	0.68	9	1.1 (0.5–2.1)	0.98	11	1.3 (0.7–2.4)	0.29
Organic solvents											
No exposure	232,212 (89)	4,489,550	61	1.0 (reference)		156	1.0 (reference)		165	1.0 (reference)	
Moderate exposure	7114 (3)	141,257	1	0.5 (0.1–3.9)		2	0.4 (0.1–1.7)		2	0.4 (0.1–1.5)	
High exposure	20,726 (8)	393,672	2	0.4 (0.1–1.8)	0.44	71	0.6 (0.3–1.2)	0.18	12	0.9 (0.5–1.6)	0.36
Wood dust											
No exposure	242,429 (93)	4,701,050	61	1.0 (reference)		152	1.0 (reference)		170	1.0 (reference)	
Moderate exposure	17,056 (7)	310,416	3	0.8 (0.2–2.5)		11	1.1 (0.6–2.0)		8	0.7 (0.4–1.5)	
High exposure	567 (–)	13,012	0	–	0.92	2	4.8 (1.2–19.4)	0.09	1	2.2 (0.3–15.9)	0.49
Dust[d]											
Unexposed	115,699 (44)	2,206,141	23	1.0 (reference)		61	1.0 (reference)		62	1.0 (reference)	
Exposed	144,353 (56)	2,818,337	41	1.2 (0.7–2.1)	0.41	104	1.1 (0.8–1.5)	0.65	117	1.2 (0.9–1.6)	0.28
Fumes[e]											
Unexposed	202,235 (78)	3,885,607	42	1.0 (reference)		127	1.0 (reference)		133	1.0 (reference)	
Exposed	57,817 (22)	1,138,872	22	1.6 (0.9–2.7)	0.08	38	0.9 (0.6–1.3)	0.70	46	1.1 (0.8–1.5)	0.69
Total[f]	260,052	5,024,479	64			165			179		

[a] In the multivariable Cox regression models adjustments were made for attained age (in 5 year-age-groups), calendar period at entry into cohort (in 3 categories; 1971–1975, 1976–1980, 1981–1993), tobacco smoking at entry into cohort (in three categories; never, previous and current), and BMI at entry into cohort (in three categories; ≤21.9 underweight, 22.0–24.9 normal, 25.0–29.9 overweight and ≥30.0 obese).

[b] The reported person-years are the numbers for the models studying esophageal adenocarcinoma. Values are slightly different for the other two outcomes due to the different end-points.

[c] Wald test of overall effect across all occupational exposure strata.

[d] Combined dust exposure is defined as either of exposure to asbestos, cement dust, concrete dust, mineral fibers, quartz dust or wood dust.

[e] Combined fume exposure is defined as either of exposure to asphalt fumes, diesel exhaust or metal fumes.

[f] Observations with missing on any covariate included in the models were excluded from the analyses.

significant associations between the other occupational exposures analyzed separately, or between the combined dust and fume exposure variables, and risk of esophageal squamous-cell carcinoma (Table 2).

Discussion

This study provides some support for the hypothesis that occupational exposures to dust and fumes may increase the risk of adenocarcinoma of the esophagus and the gastric cardia. We found positive associations between exposure to asbestos and cement dust and risk of esophageal adenocarcinoma, and between exposure to asphalt fumes and wood dust and risk of cardia adenocarcinoma. No consistent associations regarding esophageal squamous-cell carcinoma were identified.

In some occupational groups positive associations with esophageal cancer have previously been found, e.g. among workers in the rubber industry, automobile building industry workers, chimney sweeps, mine workers, individuals working with chemical products, medical X-ray workers, workers in the cement industry, plastics and composites industry workers, dye production industry workers, bookbinders, individuals with administrative jobs, health professionals, dry cleaning workers and asphalt workers [25–38]. Specific exposures and agents that have been linked with esophageal cancer include metal dust, asbestos, silica dust, combustion products, sulphuric acid, carbon black and organic solvents [39–47]. However, these studies did not distinguish between squamous-cell carcinoma and adenocarcinoma. This is a serious problem since the risk factor profiles and the descriptive epidemiology differ considerably between squamous-cell carcinoma and adenocarcinoma of the esophagus [48]. Another problem with most of these prior studies is the lack of adjustment for potential confounders [47], including the potentially important influence of tobacco smoking in studies of esophageal squamous-cell carcinoma. In the only previous study of occupations and esophageal and gastric cardia adenocarcinoma associations were found between employment in administrative support, health services, financial, insurance and real estate industries, and risk of esophageal adenocarcinoma after adjustment for smoking, alcohol and BMI [14]. For cardia adenocarcinoma associations were seen regarding employment in transportation and certain woodworking occupations [14].

The main strengths of the present study include the separate analyses of the three cancer types, the large number of participants, the long-term and complete follow-up, the prospective exposure assessment, and the availability of information on potential confounding variables. The identification of the cohort is based on a health organization with an almost complete coverage (85–90%) of individuals working in the Swedish construction industry from the beginning of the 1970s until the early 1990s [19]. The follow-up and the detection of incident cancers are complete due to the high quality and the nationwide coverage of the Swedish population-based registers used.

Some limitations of our study need consideration, where chance might be the most troublesome error. Although the men in our study accumulated five million person-years at risk, the rarity of esophageal and cardia cancers in Sweden, combined with the low prevalence of some of the occupational agents under study, resulted in a limited statistical power to ascertain weak associations. Moreover, since we tested for twelve specific and two combined occupational exposures in relation to three different cancer types we would expect two significant findings merely due to chance (with an expected number of significant results calculated as 42 comparisons * 0.05 [significance level] = 2 significant results). Another limitation is that in earlier analyses based on this cohort of construction workers the cancer incidence was lower compared to the general Swedish male population, e.g. the standardized incidence ratio for esophagus cancer was 0.66 [19]. This observation is probably due to a 'healthy worker effect', i.e. the cohort members were on average healthier compared to the male background population of the same age- and calendar period categories. This effect cannot explain our positive findings, however. Another problem is that we were unable to study lifetime occupational histories, since we only could use job title reported at the first health examination. However, in a previous study based on this cohort it was found that among construction workers examined before 1986 few subjects had changed their job tasks, and that 96.3% had the same exposure level for both previous and current job title [49]. This finding indicates that the construction industry has a stable work force, and that the lack of lifetime occupational history information did not to a large extent influence our results. Moreover, the occupational exposures included in our study are to some extent misclassified since they are based on job titles, and not on each individual's unique exposure level. Furthermore, construction workers in the unexposed groups might have been exposed, albeit at lower levels than in the exposed groups (i.e. background exposure). However, any such exposure misclassification is likely to be non-differential, i.e. be of similar levels among patients and reference participants. Therefore, this source of error should not explain our positive findings, but only dilute the effects as it introduces bias towards the null.

Finally, there were some potentially important confounding factors that we could not control for, such as alcohol consumption. However, a potential association between the studied exposures and alcohol intake in this cohort is most probably small, if it at all exists. Moreover, alcohol intake is not associated with risk of adenocarcinoma of the esophagus or gastric cardia according to recent, well-designed, population-based studies [51, 52]. For esophageal squamous-cell carcinoma, where alcohol use is a strong risk factor, any influence of high alcohol intake would to some extent indirectly be adjusted for by the adjustment for tobacco smoking.

The majority of the 12 agents in our study are particles (dust or fumes), and we hypothesized that these particles could be deposited in the airway region, inhaled or swallowed and then be deposited and act directly on the esophageal or cardia mucosa, potentially for longer periods of time. Asbestos, asphalt fumes (usually containing high amounts of polynuclear aromatic hydrocarbons [53]) and wood dust have known carcinogenic effects in the organs where they have been deposited [54, 55]. Although a limited number of our cohort members were exposed to cement dust or asbestos, the observed strong, dose–response relations between these exposures and the risk of esophageal adenocarcinoma might be of importance and deserve further attention. The findings of positive associations between high exposure to asphalt fumes and wood dust, and risk of gastric cardia adenocarcinoma may also be of importance. An increased risk of cardia adenocarcinoma was suggested for wood working occupations, such as carpenters in the construction industry, in a previous study [14]. Within highly exposed groups in the construction industry there is often one job title that is dominating. All individuals highly exposed to cement dust are found among transportation and storage workers, while insulators are highly exposed to asbestos. This latter group is also exposed to mineral fibers, which may explain the increased point estimate for mineral fibers and esophageal adenocarcinoma. In Sweden, 90% of all asbestos used was chrysotile. Before asbestos was banned in Sweden in 1976 the exposure prevalence among construction workers ought to have been much higher. This means that asbestos exposure most likely is underestimated in our cohort, resulting in the proportionately low excess of effect for cardia adenocarcinoma and esophageal squamous-cell carcinoma from asbestos exposure. Individuals exposed to asphalt fumes are road paving asphalt workers, who have relatively uniform job tasks with high asphalt fume exposure, and therefore there were no such workers in the moderately exposed group in our study. Individuals exposed to wood dust are not significantly exposed to the other 12 agents in our study. However, the low prevalence of these potential risk exposures, and the low number of cases in the exposed categories, indicate that the increasing incidence of esophageal or gastric cardia adenocarcinoma is not explained by occupational dust or fume exposure.

In conclusion, our large cohort study suggests that asbestos and cement dust exposure may be risk factors for esophageal adenocarcinoma, and that exposure to asphalt fumes and wood dust may increase the risk of gastric cardia adenocarcinoma. However, even if these associations are causal they might, at the most, only to a limited extent contribute to the major sex differences or the increasing incidence trends among patients with these tumors. More studies are needed before these observed associations can be considered established.

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