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Psychosocial working conditions and the risk of esophageal and gastric cardia cancers

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Abstract. *Background*: For reasons yet unknown, the incidence of esophageal and gastric cardia adenocarcinoma is increasing rapidly and moderately, respectively. These tumors occur predominantly among males. We hypothesized that stressful psychosocial working conditions might be involved in the etiology of these cancers. *Objective*: To study if job strain, work pace satisfaction and coping are linked to the risk of esophageal or cardia cancers. *Methods*: A nationwide Swedish population-based case–control study including 189 and 262 esophageal and cardia adenocarcinoma cases, respectively, 167 esophageal squamous-cell carcinoma cases, and 820 controls. All study subjects were interviewed. The relative risk was estimated using odds ratios, with 95% confidence intervals, adjusted for potential confounders. *Results*: We found no statistically significant associations between two different measures of job strain and the three cancer types, except between one job strain measure and risk of cardia adenocarcinoma (OR: 2.2; 95% CI: 1.0–4.8). There was a moderately strong association between having a covert coping style, compared to an overt, and risk of both esophageal (OR: 1.8; 95% CI: 1.2–2.8) and cardia adenocarcinoma (OR: 1.5; 95% CI: 1.0–2.3). Among subjects reporting low work pace satisfaction we found an almost 4-fold increased risk of esophageal squamous-cell carcinoma (OR: 3.8; 95% CI: 1.3–11.0), and a nearly 3-fold increased risk of esophageal adenocarcinoma (OR: 2.8; 95% CI: 1.1–7.0). *Conclusions*: Work-related stress does not seem to be of importance in the etiology of adenocarcinoma of the esophagus or the gastric cardia. However, the interaction of a stressful work environment and the individual's responses to it may be associated with a moderately increased risk of these cancer types.

Key words: Adenocarcinoma, Cardia cancer, Esophageal cancer, Stress, Work

Abbreviations: CI = confidence interval; OR = odds ratio

Introduction

Esophageal and gastric cardia cancers are aggressive and belong to the cancer types with the worst prognosis [1–3]. During the last few decades the incidence of adenocarcinoma of the esophagus has increased rapidly, and the incidence of gastric cardia adenocarcinoma moderately, in the United States and Western Europe, including Sweden [4–7]. There is a yet unexplained, strong male predominance among patients with adenocarcinoma of the esophagus or gastric cardia, and the rising incidence of adenocarcinomas is particularly evident among men [5, 8]. The suddenness and the rapidity of the increase [9] imply important influence of environmental exposures, probably introduced earlier than the 1970s [6, 10].

Gastroesophageal reflux [11–14] and high body mass index (BMI) [15, 16] are established risk factors for esophageal and gastric cardia adenocarcinoma, but the distribution of these factors over time and genders does not match the pattern of adenocarcinoma occurrence well. While some studies indicate that tobacco smoking might be at the most a moderate risk factor for esophageal and gastric cardia adenocarcinoma [17–19], others find no association [20]. Furthermore, smoking does not seem to explain the rising incidence of esophageal and gastric cardia adenocarcinoma among men at a time when esophageal squamous-cell carcinoma is not increasing and considering recent reductions in the prevalence of smoking, particularly among men [21]. In contrast, tobacco and alcohol use are the dominating risk factors for esophageal squamous-cell carcinoma in the Western world [22, 23]. Low consumption of fruit and vegetables is another risk factor for esophageal squamous-cell carcinoma [24], and intake of

antioxidants seems to be associated with moderately decreased risks of both adenocarcinoma and squamous-cell carcinoma of the esophagus [25]. Some data support that high intake of cereal fiber is inversely associated with risk of gastric cardia adenocarcinoma [26].

The Swedish Living Conditions Surveys (ULF) have shown increases in reports of psychologically demanding work, from 29% in 1968 [27] to 44% in 1995 [28]. Between 1981 and 1994 the Netherlands recorded an increase from 21 to 30% in the percentage of workers receiving disability pensions due to stress-related disorders [29], and according to the World Health Organization's Global Burden of Disease Survey, mental disease and stress-related disorders will be the second leading cause of disabilities in 2020 [30].

Little is known about the significance of psychosocial occupational exposures and the role of a stressful work environment in the etiology of adenocarcinoma and squamous-cell carcinoma of the esophagus, and adenocarcinoma of the gastric cardia. Only one previous study of occupational exposures has studied these three cancer types as separate diseases [31], but psychosocial occupational exposures were not included.

Stress has been defined as adaptation to different demands, following a pattern in three phases (alarm reaction, resistance and exhaustion). Severe or prolonged resistance, or defense responses, increases the risk of disease [32]. Studies have found that stress conditions can result in a short-lived rise in lower esophageal sphincter pressure, followed by relaxation and changes in esophageal motility [33]. Furthermore, chronic stress, such as work-related stress, has been associated with impaired immune function and increased susceptibility to cancer [34]. Adaptive changes resulting from chronic stress lead to a hypoactivity of the glucocorticoid receptors on immune cells and in limbic regions of the brain [34]. We hypothesized that work-related stress might decrease the pressure of the lower esophageal sphincter, thereby promoting reflux, and finally esophageal or gastric cardia adenocarcinoma, or that work-related stress could impair the immune system leading to esophageal or gastric cardia cancer.

To test these hypotheses, we used the demand–control model [35, 36], one of the most influential models in studies on health effects from psychosocial working conditions.

In addition to the demand–control model, we also evaluated if low work pace satisfaction, and passive or covert coping during a specific stressful encounter in the psychosocial work environment, might influence the risk of developing esophageal or gastric cardia cancers, in the same way as work-related stress. Coping has been suggested as an important factor in the relation between stressful events and adaptational outcomes such as depression, psychological symptoms and somatic illness [37, 38].

Our aim was to examine the relation between stressful psychosocial working conditions and the risk for cancer of the esophagus or gastric cardia in a nationwide Swedish population-based case–control study.

Materials and methods

Study design

A detailed description of our nationwide Swedish population-based case–control study has been given elsewhere [12]. The study base encompassed native Swedes younger than 80 years, and living in the country during December 1, 1994–December 31, 1997. All newly diagnosed cases of adenocarcinoma of the esophagus and gastric cardia, and half of the newly diagnosed cases of squamous-cell carcinoma of the esophagus (born on even-numbered dates) were eligible as cases. A nationwide organization for rapid case ascertainment included contact persons in all 195 departments of surgery, thoracic surgery, otorhinolaryngology, oncology and pathology, as well as continuous collaboration with the six regional tumor registries in Sweden. The control subjects were selected randomly from the Swedish total population register, and frequency matched according to the age and sex distribution of the cases of esophageal adenocarcinoma.

To reduce misclassification of the tumor site or histological type, uniform routines for documentation of the tumors were used at the participating departments. The diagnosis was based on findings at endoscopy, surgery and histopathological analysis. Finally, one pathologist reviewed biopsies and surgical specimens, or both, from 97% of the cases.

All cases and controls underwent computer-aided personal interviews performed by trained interviewers from Statistics Sweden (a government agency). A computerized questionnaire with inbuilt loops and checks for inconsistencies and errors was developed specifically for the study. The average interview time was 80 min. The majority of the interviews were conducted in the homes of the study subjects (90% of the control subjects and 66% of the case subjects), while the rest of the cases were interviewed at hospitals. Informed consent was obtained from each subject, and all regional ethics committees in Sweden approved the study.

The demand–control model

The demand–control model's two basic components are 'psychological demands' (*demands*) and 'control' (*decision latitude*). The control concept has two sub dimensions, the individual's possibilities to use and develop one's skills (*skill discretion*) and the individual's possibility to influence decision-making (*deci-*

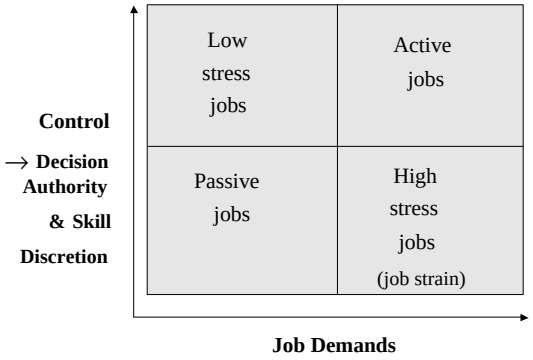

Figure 1. The demand–control model [36].

sion authority). Skill discretion and decision authority are highly correlated and therefore merged into the control dimension [35, 36].

The demand–control model distinguishes between four types of work: (1) 'High stress jobs', with a combination of high demands and low control, i.e. *job strain*; (2) 'active jobs' with high demands and high control; (3) 'low stress jobs' with low demands and high control and (4) 'passive jobs', low in both demands and control (Figure 1). The model assumes that persons exposed to job strain may have an increased risk of psychological strain and health problems [39]. This has been tested empirically for several health outcomes such as cardiovascular disease [40–43], mental health [44–46] and sickness absenteeism [47]. Later, the dimension 'social support at the workplace' was added to the model, assuming that it has a risk-modifying effect, where the hypothesis is that the highest risk for illness can be found in the group with high demands, low control and low social support [48].

Data on psychosocial working conditions

The study questionnaire contained 15 questions addressing the subject's psychosocial work environment during the 1970s, i.e. about 20 years before the diagnosis of cancer was confirmed and the data collected. We choose to assess exposure 20 years before the diagnosis of cancer since this is a reasonable latency period between an exposure and the fully developed invasive cancer of the esophagus or gastric cardia. Included were the dimensions demands, control (i.e. decision authority and skill discretion[1]), social support[2], work pace satisfaction and coping.

Detailed descriptions of the questions used for the different indices are given in Appendix A. To evaluate job strain we used a previously employed method [49] to construct three indices, two for the dimension authority over decisions and one for the dimension job demands (Appendix). Authority over decisions was measured in two different ways. First, labeled '*authority specific*', three questions were used to construct a variable describing freedom over one's schedule at work, dichotomized into low (exposed) and high (unexposed) authority over decisions. Secondly, labeled '*authority general*', two questions were used for measuring a more general definition of authority over decisions, describing influence over one's work pace and how the work tasks should be performed. This variable was also dichotomized into low (exposed) and high (unexposed) authority over decisions. Two questions were used to obtain a measure of *demands*, where the response alternatives were dichotomized into high (exposed) and low (unexposed) demands.

Finally, these three indices were used to construct two different job strain variables according to Karasek's demand–control (job strain) model [35, 36]. For one, labeled '*job strain specific*', we combined high demands with low 'authority specific', dichotomized as described above. For the other, labeled '*job strain general*', we combined high demands with low 'authority general'. In the analyses, we compared the group with 'high stress jobs' (job strain) with all the other groups combined (i.e. those with active jobs, low stress jobs and passive jobs).

Similar methods were used for the dimensions work pace satisfaction and coping, respectively (Appendix). One question was dichotomized into low (exposed) and high (unexposed) work pace satisfaction. Another question, based on items previously used in studies of coping with unfair treatment at work [38, 50], was dichotomized into covert (exposed) and overt (unexposed) coping.

Statistical analyses

Using conditional logistic regression, odds ratios and their 95% confidence intervals were estimated by the maximum-likelihood method [51]. Data were analyzed using the PHREG procedure in SAS [52]. In multivariate models, adjustments were made for six potentially confounding factors: Reflux symptoms (yes or no), BMI (in four categories based on quartiles), alcohol use (yes or no), tobacco smoking (in three categories), educational level (in three categories) and dietary intake of fruit and vegetables (in three categories). We also evaluated potential confounding of living with a partner (cohabitant or married), but found no confounding effects and left this variable out of the final models.

If reflux were in the causal path in the etiology of esophageal and gastric cardia adenocarcinoma, any observed associations between work-related stress and the outcome would be reduced when controlling

[1]We did not have an adequate measure for skill discretion, and therefore this dimension was not included in the analyses.

[2]For the social support dimension, two questions were dichotomized into low (exposed) and high (unexposed) social support, but too few subjects were exposed (six cases, three controls) to allow analyses.

for reflux, and should not be included in any statistical models. We therefore compared relative risk estimates from models both including and excluding reflux symptoms.

Results

Participation rates and characteristics of the study subjects

The study included 189 cases with esophageal adenocarcinoma, 262 with gastric cardia adenocarcinoma and 167 with esophageal squamous-cell carcinoma. They constituted 88, 84 and 73% respectively, of all eligible cases in the study base. The 820 control persons constituted 73% of all who had been primarily selected. The reasons for non-participation along with other characteristics of the participants are presented in Table 1. The majority of the subjects were men between 60 and 79 years old. About half of the subjects within each case group and 39% among the controls had 7–10 years of formal education (medium level). The majority (79–85%) of all subjects were married or cohabitant during the mid 1970's.

Distribution of psychosocial working conditions

The distribution of psychosocial working conditions among the study subjects is presented in Table 2. Among both the control subjects and the cases of esophageal adenocarcinoma and squamous-cell carcinoma 11% reported a *low degree of authority over decisions* (*specific authority*), while the frequency of this exposure among the cases of gastric cardia adenocarcinoma was lower (6%). Exposure to *a low degree of authority over decisions* (*general authority*) was found among 8% of the controls, and within 10–11% of all three case groups. The percentages of subjects who reported *high job demands* was 27, 23, 31 and 29 among control subjects, cases of esophageal adenocarcinoma, gastric cardia adenocarcinoma and esophageal squamous-cell carcinoma, respectively. The frequency of subjects exposed to *job strain* (both *specific* and *general job strain*) was similar among the case groups and the controls (2–5%) (Table 2).

While only 2% of the control subjects reported *low work pace satisfaction*, the corresponding distribution among the cases of esophageal adenocarcinoma, gastric cardia adenocarcinoma and esophageal squamous-cell carcinoma was 6, 4 and 5%, respectively (Table 2).

The use of *covert coping* was found among 16% of the control subjects, while the percentages among the cases with esophageal adenocarcinoma, gastric cardia adenocarcinoma and esophageal squamous-cell carcinoma were 26, 21 and 19, respectively (Table 2).

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The results of the multivariate analyses are shown in Tables 3–5. Persons not answering all questions that were part of the indices were excluded in the analyses (Tables 3–5). The percentages of missing subjects varied between 1 and 9, and there were no major differences between the cases and the controls (Table 2).

Decision authority, job demands and job strain

No statistically significant associations were found between the dimensions *low authority over decisions* (both measures) or *high job demands* and risk for any of the three cancer types, except for an inverse association of having *low authority over decisions* (*specific authority*) and risk of gastric cardia adenocarcinoma (OR, both with and without adjustment for reflux symptoms, 0.5; 95% CI: 0.3–0.9) (Table 3).

Furthermore, we found no statistically significant associations between the two different measures of *job strain* exposure and the risk of adenocarcinoma of the esophagus (OR: 0.5; 95% CI: 0.2–1.6 for *job strain specific*, OR: 1.9; 95% CI: 0.7–5.2 for *job strain general*), adenocarcinoma of the gastric cardia (OR: 0.4; 95% CI: 0.1–1.1 for *job strain specific*), or squamous-cell carcinoma of the esophagus (OR: 0.6; 95% CI: 0.2–1.8 for *job strain specific*, OR: 0.8; 95% CI: 0.2–2.4 for *job strain general*) (Tables 4 and 5). The OR's and their 95% CI's were identical or similar with or without adjustment for reflux (Tables 4 and 5), except for a statistically significant positive association between *job strain general* and risk of gastric cardia adenocarcinoma that was seen when not adjusting for reflux (OR: 2.2; 95% CI: 1.0–4.8) (Table 5).

Work pace satisfaction

We found an almost 4-fold significantly increased risk of esophageal squamous-cell carcinoma among persons with *low work pace satisfaction* compared to persons with high work pace satisfaction (OR: 3.8; 95% CI: 1.3–11.0 in the model including *job strain specific*, OR: 3.6; 95% CI: 1.3–10.4 in the model including *job strain general*) (Tables 4 and 5).

We found a nearly 3-fold significantly increased risk of esophageal adenocarcinoma among persons reporting *low work pace satisfaction* compared to persons with high work pace satisfaction (OR: 2.8; 95% CI: 1.1–7.0 in the model including *job strain specific*, OR: 2.6; 95% CI: 1.0–6.5 in the model including *job strain general*) (Tables 4 and 5). These associations disappeared when adjusting for reflux (Tables 4 and 5).

Coping

For persons not taking any action when treated unfairly at work (*covert coping*), the risk of esophageal

Table 1. Characteristics of the study subjects

Characteristic	Adenocarcinoma of esophagus, N (%)	Adenocarcinoma of gastric cardia, N (%)	Squamous-cell carcinoma of esophagus, N (%)	Controls N (%)
Number of participants (percent of all eligible)	189 (88)	262 (84)	167 (73)	820 (73)
Reasons for non-participation (percent of all eligible)				
Unwillingness	2 (1)	10 (3)	11 (5)	210 (19)
Physical/mental disorders or early death	25 (12)	41 (13)	50 (22)	70 (6)
Age groups				
–49	7 (4)	26 (10)	3 (2)	48 (6)
50–59	31 (16)	49 (19)	35 (21)	161 (20)
60–69	61 (32)	84 (32)	67 (40)	245 (30)
70–79	90 (48)	103 (39)	62 (37)	366 (45)
Sex				
Male	165 (87)	223 (85)	120 (72)	679 (83)
Female	24 (13)	39 (15)	47 (28)	141 (17)
Educational level				
Low (0–6 years)	48 (25)	43 (16)	41 (24)	182 (22)
Medium (7–10 years)	94 (50)	126 (48)	78 (47)	317 (39)
High (<10 years)	47 (25)	93 (36)	48 (29)	321 (39)
Living with partner (married/cohabitant)				
Yes	149 (79)	221 (84)	133 (80)	698 (85)
No	14 (7)	24 (9)	16 (9)	79 (10)
Missing	26 (14)	17 (7)	18 (11)	43 (5)
Smoking (including all use of tobacco)				
Never	57 (30)	43 (16)	22 (13)	325 (40)
Previous	89 (47)	124 (47)	44 (26)	314 (38)
Current (2 years before interview)	43 (23)	95 (36)	101 (60)	181 (22)
Heavy alcohol drinkers[a]				
Yes	43 (23)	76 (29)	78 (47)	178 (22)
No	146 (77)	186 (71)	89 (53)	642 (78)
Body mass index[b]				
Quartile I: 16.5–22.0	12 (6)	50 (19)	51 (30)	205 (25)
Quartile II: 22.1–23.7	26 (14)	46 (18)	34 (20)	207 (25)
Quartile III: 23.8–25.4	53 (28)	65 (25)	35 (21)	203 (25)
Quartile IV: 25.5–40.2	98 (52)	101 (38)	47 (28)	201 (25)
Missing				4 (–)
Reflux symptoms[c]				
Yes	113 (60)	75 (29)	25 (15)	135 (16)
No	76 (40)	187 (71)	142 (85)	685 (84)
Intake of fruit and vegetables[d]				
Least	69 (36.5)	97 (37)	62 (37)	217 (26)
Medium	69 (36.5)	98 (37)	56 (34)	327 (40)
Highest	51 (27)	67 (26)	49 (29)	276 (34)

[a] Defined as more than 70 g of alcohol/week, 20 years ago.
[b] In four categories, based on quartiles among the controls, 20 years ago. BMI calculated as bodyweight in kilograms divided by the square of body height in meters (kg/m^2).
[c] Heartburn and/or regurgitation at least 50 times/year, in sum 1 year of subject's life.
[d] Frequency of intake of fruit and vegetables on average per week in three categories; least, medium, highest, 20 years ago.

adenocarcinoma was almost 2-fold significantly increased compared to persons who reacted openly in some way (Appendix) when treated unfairly (*overt coping*) (OR: 1.8; 95% CI: 1.2–2.8 for both the model including *job strain specific* and *job strain general*). For gastric cardia adenocarcinoma the corresponding risk was moderately increased (OR: 1.5; 95% CI: 1.0–2.3 for the model including *job strain specific*, OR: 1.5; 95% CI: 1.0–2.2 for the model including *job strain general*). No association was identified between *coping style* and risk of esophageal squamous-cell carcinoma (Tables 4 and 5). The point estimates for the associations between covert coping and esophageal adenocarcinoma were marginally elevated after

Table 2. Distribution of psychosocial working conditions among the study subjects

Work condition	Adenocarcinoma of esophagus, N (%) total 189	Adenocarcinoma of gastric cardia N (%) total 262	Squamous-cell carcinoma of esophagus N (%) total 167	Controls N (%) total 820
Authority over decisions[a]				
Authority specific				
Unexposed (high)	165 (87)	235 (90)	143 (86)	703 (86)
Exposed (low)	20 (11)	16 (6)	18 (11)	93 (11)
Missing	4 (2)	11 (4)	6 (3)	24 (3)
Authority general				
Unexposed (high)	166 (88)	227 (87)	146 (87)	739 (90)
Exposed (low)	19 (10)	28 (11)	19 (11)	69 (8)
Missing	4 (2)	7 (3)	2 (1)	12 (1)
Demands[b]				
Unexposed (low)	141 (75)	173 (66)	115 (69)	587 (72)
Exposed (high)	43 (23)	82 (31)	48 (29)	222 (27)
Missing	5 (3)	7 (3)	4 (2)	11 (1)
Job strain[c]				
Job strain specific				
No	179 (95)	245 (93)	153 (92)	761 (93)
Yes	4 (2)	5 (2)	6 (3)	34 (4)
Missing	6 (3)	12 (5)	8 (5)	25 (3)
Job strain general				
No	178 (94)	241 (92)	158 (95)	784 (96)
Yes	6 (3)	13 (5)	5 (3)	23 (3)
Missing	5 (3)	8 (3)	4 (2)	13 (1)
Work pace satisfaction[d]				
Unexposed (high)	175 (93)	246 (94)	156 (93)	794 (97)
Exposed (low)	11 (6)	10 (4)	8 (5)	16 (2)
Missing	3 (1)	6 (2)	3 (2)	10 (1)
Coping[e]				
Unexposed (overt coping)	126 (67)	184 (70)	124 (74)	627 (76)
Exposed (covert coping)	50 (26)	55 (21)	32 (19)	134 (16)
Missing	13 (7)	23 (9)	11 (7)	59 (7)

[a] Two different measures: (1) *Authority specific*, describing freedom over one's schedule at work (three questions dichotomized as high and low authority specific). (2) *Authority general*, describing influence over one's work pace and how the work tasks should be performed (two questions dichotomized as high and low authority general).
[b] *Demands*, describing job demands (two questions dichotomized as low and high demands).
[c] Two different measures, both combining high demands and low authority over decisions (dichotomized as no/yes): (1) *Job strain specific* (including authority specific). (2) *Job strain general* (including authority general).
[d] *Work pace satisfaction*, describing satisfaction with work pace (one question dichotomized as high and low work pace satisfaction).
[e] *Coping*, describing coping with unfair treatment at work (one question dichotomized as overt and covert coping).

adjusting for reflux (OR: 2.1; 95% CI: 1.3–3.4 for the model including *job strain specific*, OR: 2.1; 95% CI: 1.3–3.3 for the model including *job strain general*), while no influence of reflux on the associations between coping style and risk of gastric cardia adenocarcinoma and esophageal squamous-cell carcinoma was seen (Tables 4 and 5).

Each of the 15 questions regarding psychosocial working conditions was also analyzed separately. Only a few, possibly spurious significant associations were found (data not shown).

Discussion

Our study revealed no associations between job strain and risk of adenocarcinoma of the esophagus or gastric cardia, except for a positive association between one job strain measure and the risk of gastric cardia adenocarcinoma. However, we found a moderately strong association between having a covert coping style when treated unfairly at work and the risk of both these tumors. Among subjects reporting low work pace satisfaction we found an increased risk of both adenocarcinoma and squamous-cell carcinoma of the esophagus.

Our finding of an increased risk of esophageal and gastric cardia adenocarcinoma among individuals reporting a covert coping style is interesting, but this is the only study presenting such data and this finding must be interpreted cautiously. In a Swedish cross-sectional study, it was found that high scores of covert coping were associated with a 60% increased

Table 3. Decision authority, and job demands and risk of esophageal and gastric cardia cancers[a]

	Adenocarcinoma of esophagus			Adenocarcinoma of gastric cardia			Squamous-cell carcinoma of esophagus		
	Cases/controls	OR	(95% CI)	Cases/controls	OR	(95% CI)	Cases/controls	OR	(95% CI)
Authority specific									
Unexposed (high)	165/700	1.0	(reference)	235/700	1.0	(reference)	143/700	1.0	(reference)
Exposed (low)	20/93	0.6	(0.3–1.2)	16/93	0.5	(0.3–0.9)	18/93	1.0	(0.5–1.8)
		0.8[b]	(0.5–1.4)		0.5[b]	(0.3–0.9)		1.0[b]	(0.5–1.8)
Authority general									
Unexposed (high)	166/736	1.0	(reference)	227/736	1.0	(reference)	146/736	1.0	(reference)
Exposed (low)	19/68	1.0	(0.5–2.0)	28/68	1.3	(0.8–2.1)	19/68	1.3	(0.7–2.4)
		1.4[b]	(0.8–2.5)		1.4[b]	(0.8–2.3)		1.3[b]	(0.7–2.4)
Demands									
Unexposed (low)	141/584	1.0	(reference)	173/584	1.0	(reference)	115/584	1.0	(reference)
Exposed (high)	43/221	0.7	(0.4–1.1)	82/221	1.2	(0.8–1.6)	48/221	1.0	(0.7–1.6)
		0.8[b]	(0.5–1.2)		1.2[b]	(0.9–1.7)		1.0	(0.7–1.6)

[a] In the multivariate logistic regression models adjustments were made for reflux symptoms, BMI (quartiles), alcohol use, tobacco smoking, educational level and intake of fruit and vegetables.
[b] In the multivariate logistic regression models adjustments were made for BMI (quartiles), alcohol use, tobacco smoking, educational level and intake of fruit and vegetables, excluding reflux symptoms.

prevalence of hypertension in men, but not in women [38]. Furthermore, in a case–control study in the United States, hypertension was associated with a 2-fold increased risk of adenocarcinomas of the esophagus and gastric cardia [17].

Antihypertensive drugs, relaxing the lower esophageal sphincter, may conceivably explain the increased risk of these cancers associated with hypertension, but a common underlying factor remains a possibility. We have previously provided evidence that long-term use of medications relaxing the lower esophageal sphincter may increase the risk of esophageal adenocarcinoma [53]. A sphincter relaxing effect could be a mechanism explaining also the association between covert coping and esophageal and gastric cardia adenocarcinoma.

Table 4. Work pace satisfaction, coping, and job strain (specific) and risk of esophageal and gastric cardia cancers[a]

	Adenocarcinoma of esophagus			Adenocarcinoma of gastric cardia			Squamous-cell carcinoma of esophagus		
	Cases/ controls	OR	(95% CI)	Cases/ controls	OR	(95% CI)	Cases/ controls	OR	(95% CI)
Work pace satisfaction									
Unexposed (high)	175/791	1.0	(reference)	246/791	1.0	(reference)	156/791	1.0	(reference)
Exposed (low)	11/15	1.5	(0.6-4.3)	10/15	1.4	(0.6-3.4)	8/15	3.8	(1.3-10.9)
		2.8[b]	(1.1–7.0)		1.7[b]	(0.7–4.2)		3.8[b]	(1.3–11.0)
Coping									
Unexposed (overt coping)	126/624	1.0	(reference)	184/624	1.0	(reference)	124/624	1.0	(reference)
Exposed (covert coping)	50/133	2.1	(1.3–3.4)	55/133	1.6	(1.1–2.3)	32/133	1.3	(0.8–2.3)
		1.8[b]	(1.2–2.8)		1.5[b]	(1.0–2.3)		1.3[b]	(0.8–2.3)
Job strain specific									
No	179/759	1.0	(reference)	245/758	1.0	(reference)	153/758	1.0	(reference)
Yes	4/34	0.4	(0.1–1.3)	5/34	0.4	(0.1–1.1)	6/34	0.7	(0.2–1.8)
		0.5[b]	(0.2–1.6)		0.4[b]	(0.1–1.1)		0.6[b]	(0.2–1.8)

[a] In the multivariate logistic regression models adjustments were made for all other psychosocial working conditions in the table, and reflux symptoms, BMI (quartiles), alcohol use, tobacco smoking, educational level and intake of fruit and vegetables.
[b] In the multivariate logistic regression models adjustments were made for all other psychosocial working conditions in the table, and BMI (quartiles), alcohol use, tobacco smoking, educational level and intake of fruit and vegetables, excluding reflux symptoms.

Table 5. Work pace satisfaction, coping, and job strain (general) and risk of esophageal and gastric cardia cancers[a]

	Adenocarcinoma of esophagus			Adenocarcinoma of gastric cardia			Squamous-cell carcinoma of esophagus		
	Cases/ controls	OR	(95% CI)	Cases/ controls	OR	(95% CI)	Cases/ controls	OR	(95% CI)
Work pace satisfaction									
Unexposed (high)	175/791	1.0	(reference)	246/791	1.0	(reference)	156/791	1.0	(reference)
Exposed (low)	11/15	1.4	(0.5–3.9)	10/15	1.1	(0.4–2.9)	8/15	3.6	(1.2–10.3)
		2.6[b]	(1.0–6.5)		1.4[b]	(0.6–3.5)		3.6[b]	(1.3–10.4)
Coping									
Unexposed (overt coping)	126/624	1.0	(reference)	184/624	1.0	(reference)	124/624	1.0	(reference)
Exposed (covert coping)	50/133	2.1	(1.3–3.3)	55/133	1.5	(1.0–2.3)	32/133	1.4	(0.8–2.3)
		1.8[b]	(1.2–2.8)		1.5[b]	(1.0–2.2)		1.4[b]	(0.8–2.3)
Job strain general									
No	178/781	1.0	(reference)	241/781	1.0	(reference)	158/781	1.0	(reference)
Yes	6/22	1.5	(0.5–4.7)	13/22	2.0	(0.9–4.5)	5/22	0.8	(0.2–2.4)
		1.9[b]	(0.7–5.2)		2.2[b]	(1.0–4.8)		0.8[b]	(0.2–2.4)

[a] In the multivariate logistic regression models adjustments were made for all other psychosocial working conditions in the table, and reflux symptoms, BMI (quartiles), alcohol use, tobacco smoking, educational level and intake of fruit and vegetables.

[b] In the multivariate logistic regression models adjustments were made for all other psychosocial working conditions in the table, and BMI (quartiles), alcohol use, tobacco smoking, educational level and intake of fruit and vegetables, excluding reflux symptoms.

The somewhat surprising finding of an inverse association between low decision authority (specific authority) and gastric cardia adenocarcinoma is in contrast to studies of other diseases. A negative change in decision authority, in men, has been reported as an important risk factor for myocardial infarction [42]. One explanation for our finding could be that persons reporting low decision authority (specific authority) have a personal preference for experiencing these working conditions as comfortable, not stressful. This is in accordance with the so-called person-environment fit model, which states that strain develops when there is disagreement between the person and the environment [54]. Still, it is unlikely that the distribution of this personal preference is so skewed, leaving chance as the most likely explanation for this result. We tested for multiple exposures and three cancer types, and would expect statistically significant associations due to chance only. Chance might be the most likely explanation for the finding of a positive association between 'job strain general' and gastric cardia adenocarcinoma.

The association between low work pace satisfaction and risk of esophageal squamous-cell carcinoma could be due to stress responses affecting the immune system, with a subsequently increased cancer risk [34]. Other potential explanations include residual confounding or chance.

The finding among subjects reporting low work pace satisfaction of an almost 3-fold increased risk of esophageal adenocarcinoma, when not including reflux symptoms in the statistical models, might be explained by an increased occurrence of reflux secondary to stress responses [33].

The strengths of this study are the use of a population-based design, a uniform classification of the tumor types, and a complete and rapid case ascertainment that made it possible to perform personal interviews with all study subjects. The personal interviews increased the validity of the exposure data and reduced the number of individuals not answering all questions. Furthermore, the subjects were not aware of the hypothesis of work-related stress in relation to these cancer types.

A weakness of our study is the low frequency of individuals identified as being exposed to job strain (2–5%), fewer than expected compared to previous studies (10–40%) [55]. This reduced the statistical power to detect weak associations. One possible explanation for the low prevalence of job strain could be the retrospective data collection, where subjects may underreport job strain when answering questions about their work situation 20 years ago. However, in one Swedish study of the validity of retrospective data collection of psychosocial working conditions, no major differences between retrospective or prospective data collection were found [56]. Another explanation could be that our definition of job strain is stricter than the methods used most frequently in psychosocial occupational research. Usually there are scales of questions where the subjects' responses are calculated as scores. Our method may have resulted in fewer individuals being classified as exposed. If there exists an underestimation of exposure in our study, this misclassification of exposure is likely to be non-differential (the same for cases and controls) and should influence the relative risk estimates towards the null.

We might have misclassified job strain since we were unable to use the entire control dimension (including both skill discretion and decision authority). We only used decision authority, as skill discretion was not satisfactorily covered in the study questionnaire. However, we do not believe this influenced the results to a great extent, since the correlation between these two dimensions is usually very high [36]. The differences in the risk estimates for the different measures of job strain, i.e. job strain including authority specific and job strain including authority general, might be of interest. The OR for esophageal and gastric cardia adenocarcinoma, unadjusted for reflux symptoms, was 0.5 and 0.4 for job strain specific, compared to 1.9 and 2.2 for job strain general, respectively. Authority specific concerns personal freedom over a work schedule; freedom to make telephone calls, receive private visitors and leave the job for shorter periods. This may have a different meaning than authority general, concerning influence over work pace and how the work should be performed, perhaps more important aspects of decision authority.

In conclusion, this study suggests that work-related stress does not seem to be of importance in the etiology of adenocarcinoma of the esophagus or the gastric cardia. However, the interaction of a stressful work environment and the individual's responses to it may be associated with a moderately increased risk of these cancer types, a finding that warrants further studies.

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Appendix A

The following method, according to Karasek and colleagues [49], was used to construct three indices, two for the dimension decision authority and one for the dimension job demands. These indices were then used to construct two different job strain variables, combining high demands with low decision authority.

Decision authority

Authority over decisions was measured in two different ways:

(1) The following three questions were used to measure 'the personal schedule freedom' [49], labeled *authority specific*, describing freedom over one's schedule at work:
   – Could you make at least one private telephone call during regular working hours?
   – Could you receive a private visitor for 10 min during regular working hours?
   – Could you leave your job for half-an-hour for private errands during working hours without telling your supervisor?

   Two response alternatives: (a) yes and (b) no

   These questions were dichotomized as

Low authority (*exposed*): Response 'no' to all three questions.

High authority (*unexposed*): Response 'yes' to at least one of the three questions.

(2) The following two questions were used to measure a more general description of authority over decisions (from Theorell's Swedish demand–control-support scale), labeled *authority general*, describing influence over one's work pace and how the work tasks should be performed:
   – Did you decide your work pace yourself?
   – Did you have freedom to decide how your work should be performed?

   Four response alternatives: (a) always or almost always, (b) often, (c) seldom and (d) never.

   These questions were dichotomized as:

Low authority (*exposed*): Response 'seldom/never' to both questions.

High authority (*unexposed*): Response 'always/often' to at least one of the two questions.

Job demands

The following two questions were used for the *job demands* [49] measure:
   – What work pace did you have in your work an ordinary working day?

   Three response alternatives: (a) high work pace, (b) medium work pace and (c) low work pace.
   – Was your work psychologically demanding?

   Four response alternatives: (a) always or almost always, (b) often, (c) seldom and (d) never.

   These two questions were dichotomized as

High demands (*exposed*): Response 'high work pace' to the first question, 'always/often' to the second question.

Low demands (*unexposed*): Response 'medium/low work pace' to the first question and/or 'seldom/never' to the second question.

The following two dimensions concerning work pace satisfaction and coping style were not part of the job strain variables:

Work pace satisfaction

The following question was used to measure *work pace satisfaction*.
   – Were you satisfied with your work pace?

   Four response alternatives: (a) good, (b) rather good, (c) rather bad and (d) bad.

   This question was dichotomized as

Low satisfaction (*exposed*): Response 'rather bad/bad' to the question.

High satisfaction (*unexposed*): Response 'rather good/good' to the question.

Coping

The following question was used to measure *coping with unfair treatment at work* [38].

– How did you usually react when you were treated in an unfair way or got into conflict with a colleague? Even if you seldom or never got into conflict we would like you to note how you would have reacted.

There were five response alternatives: (a) let it pass without saying anything, (b) protested directly, (c) talked with the person right away, (d) yelled at the person right away, (e) spoke to the person later when you had calmed down.

This question was dichotomized as:

Covert coping (*exposed*): Response (a) to the question.

Overt coping (*unexposed*): Response (b), (c), (d) or (e) to the question.

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