Available online at www.sciencedirect.com

SciVerse ScienceDirect

journal homepage: http://www.kjms-online.com

ORIGINAL ARTICLE

Occupational risks of esophageal cancer in Taiwanese men

Shih-Hui Huang [a], I-Chen Wu [b], Deng-Chyang Wu [b], Chun-Chieh Wu [c], Jeng-Fu Yang [d], Yu-Kuei Chen [e], Chee-Yin Chai [c], Yu-Wen Chiu [f,g], Chia-Tsuan Huang [f,g], Tzu-Chi Lee [a], Ming-Tsang Wu [a,g,*]

[a] Department of Public Health, College of Health Sciences, Kaohsiung Medical University, Kaohsiung, Taiwan
[b] Division of Gastroenterology, Department of Internal Medicine, Kaohsiung Medical University Hospital, Kaohsiung Medical University, Kaohsiung, Taiwan
[c] Department of Pathology, Kaohsiung Medical University Hospital, Kaohsiung, Taiwan
[d] Department of Preventive Medicine, Kaohsiung Medical University Hospital, Kaohsiung, Taiwan
[e] Department of Food Science and Nutrition, Meiho University, Pingtung, Taiwan
[f] Department of Family Medicine, Kaohsiung Medical University, Kaohsiung, Taiwan
[g] Department of Family Medicine, Kaohsiung Medical University Hospital, Kaohsiung, Taiwan

Abstract   This study aims to explore whether certain occupations were associated with the risk of esophageal squamous cell carcinoma (ESCC) in Taiwan. In a hospital-based case-control study, we collected 326 newly diagnosed ESCC patients and 386 age-matched controls (the ratio of case patients: controls = 1:1—2). All respondents completed a questionnaire, including 33 occupations in which environments potential exposure to cancer-related hazards are present. Workers with dust and metal exposure were categorized into Groups A and B, respectively. Relative risks for ESCC were estimated by odds ratios adjusting for covariates (AOR). Compared with the controls, farmer/gardener (AOR = 2.08, 95% CI = 1.02—4.24) and workers in Group A (AOR = 2.80, 95% CI = 1.21—6.47) had significantly higher risk for developing ESCC. A tendency of increased risk was also found in workers in group B (OR = 5.72 95% CI = 2.33—14.03), but such association was not significant after adjusting for other covariates (AOR = 1.57, 95% CI = 0.54—6.61). Our results suggested that farmer/ gardener and workers with exposure to dust had a significant excess risk of ESCC. This study added further evidence to the current knowledge that occupational hazards are important in the development of ESCC.
Copyright © 2012, Elsevier Taiwan LLC. All rights reserved.

  * Corresponding author. Department of Family Medicine, Kaohsiung Medical University Hospital, No. 100, Shih-Chuan 1st Road, Kaohsiung 807, Taiwan.
    E-mail address: 960021@ms.kmuh.org.tw (M.-T. Wu).

Introduction

Esophageal cancer ranks as the eighth most common malignancy worldwide [1]. Its incidence among men is about 10 times higher than that among women. However, the change in epidemiology varies greatly from country to country in the past few decades [1]. In most areas, especially in Asia, esophageal squamous cell carcinoma (ESCC) remains the predominant histologic type, while in many developed countries the incidence of adenocarcinoma increased dramatically and surpassed that of ESCC. In opposite to that in Western countries, more than 95% of esophageal cancer in Taiwan is ESCC and the incidence is still increasing. In 2007, the age-adjusted incidence and mortality rate of esophageal cancer soared to 12 and 9.6 per 100,000, respectively, among Taiwanese men [2]. Such geographic variations may imply that different etiologies of esophageal cancer exist in different areas.

In addition to smoking and alcohol drinking, two well-established ESCC risk factors worldwide, our previous studies also linked areca chewing to the presence of ESCC in Taiwan [3–5]. Besides these three important risk factors (tobacco, alcohol, and areca nut), the occupational distribution may provide more clues to other unknown etiologies of ESCC. A growing body of evidence has indicated that exposure to industry-related chemicals, such as sulfuric acid, and carbon black and silica dust may increase ESCC risk [6–8]. A Swedish case-control study also found concrete/construction workers and hotel/restaurant workers were at a significantly higher risk of ESCC [9]. However, few reports examined the occupational factors of ESCC among the high-prevalent Chinese populations, especially the Taiwanese. In this study, we aim to investigate the association of occupations and male ESCC in a highly industrialized city of southern Taiwan.

Materials and methods

The sample for this study was obtained from a previous multi-centered hospital-based case-control study [3–5]. Briefly, a survey covering demographic information, job history, and substance use (tobacco, alcohol and areca nut) was administered to 326 male patients with newly diagnosed and histologically proved with ESCC from Kaohsiung Medical University Hospital (KMUH) and Kaohsiung Veterans General Hospital, two academic medical centers in a highly industrialized city, Kaohsiung, located in southern Taiwan from 2000 to 2006. A total of 386 age-matched (±4 years) healthy male controls were recruited from the Department of Preventive Medicine for health checkups in the two medical centers. (case patients: controls = 1:1 or 1:2) The response rate of subjects was more than 95% of those originally recruited [3]. This study was approved by the Institutional Review Boards of KMUH (KMUH-IRB-930010). Informed consent was obtained from all participants.

Questionnaire

Detailed personal interview information on demographic characteristics, history of tobacco, alcohol and areca consumption as well as lifetime occupational history was obtained from all participants. Respondents who had smoked more than 10 cigarettes per week for at least 6 months were defined as cigarette smokers. Those who had drunk beer, wine or distilled spirits more than once a week for at least 6 months were defined as alcoholic beverage drinkers. In addition, participants who reported regularly chewing betel quid for at least 6 months were defined as areca chewers [3–5].

For items of occupational history, we asked whether the participants were working or had worked at least one year in any of 33 different common occupations whose environments are known to have potential exposure to hazards related to cancer development in Taiwan. Occupations with similar hazardous exposure were categorized into one work group. Carpenter, woodcutter, road/concrete constructer, and shipbuilding or breaking worker have common exposure to dusts (e.g., wood dust and crystalline silica) and were categorized into work Group A [7,10]. Iron/steel company workers, motor vehicle mechanics/repairers, painters, and welders were exposed to welding fumes or metals such as aluminum, iron, lead, chromium, and metallic dust; therefore, they were categorized into work Group B [7]. Other occupations included farmer/gardener, petrochemical worker, plastic worker, quarryman, leather maker, weaver, coking worker, paper-making worker, incense manufacturing worker, tobacco manufacturing worker, brewer, hairdresser, bird keeper, carpet worker, gas station worker, asbestos-related worker, firefighter, aluminum worker, incinerator worker, coal miner, irradiation technologist, nuclear power plant worker, and oil painter.

Statistical analysis

Student t-statistics for the continuous variable and χ^2 or Fischer's exact test for the categoric variable were applied to analyze the distribution of demographic data and occupation-related variables by the status of case/control. Univariate and multivariate logistic regression were used to examine the relationship between an occupation variable and the presence of ESCC. Adjusted odds ratio (AOR) of the potentially significant occupations were obtained after controlling for potential confounders or significant risk factors in the univariate analysis, including education levels (≤primary school, high schools and ≥ college), smoking (yes/no), alcohol drinking (yes/no), and areca chewing (yes/no). The significant variables of occupations were further examined their effect of duration of employment (years) dichotomized by median on the risk of ESCC in the multivariate models. The synergistic interactions between the significant variable of occupation and other covariates, including education levels, smoking, alcohol drinking, or areca chewing, were also explored. Since the synergistic effects did not reach the statistical significance, the final models only included the main determinants. Data were analyzed using the SAS statistical package; all p values were two-sided and the significance of <0.05.

Results

Mean age in case group was 57.98 years of age, which was not significantly different from that in the control group

(Table 1). By contrast, low educational level and substance use (tobacco, alcohol and areca) were significantly associated with the presence of ESCC (all p values < 0.0001). Table 2 shows the relationship between occupations and ESCC risk. Ten of the 33 occupations did not have any representative workers in both case and control groups and, thus, they were not included for the subsequent analyses. Although many of the remaining occupations have very few representative workers, we found that farmer/gardener and workers in Group A (occupations with dust exposure) and Group B (occupations with metal exposure) had the significant increased risk of ESCC (Table 2).

After adjusting for other covariates, we still found that farmers/gardeners (AOR = 2.08, 95% CI = 1.02–4.24; p = 0.04) and workers in Group A (AOR = 2.80, 95% CI = 1.21–6.47; p = 0.02) remained significant (Table 3). By contrast, workers in Group B were not significant anymore after adjusting for other covariates (AOR = 1.57, 95% CI = 0.54–6.61; p = 0.41). For the other covariates, we found that the p-values of them, including education levels, cigarette smoking, alcohol drinking, and areca nut chewing were still significant (p < 0.0001) in the final models.

We further examined the effect of duration of employment of farmers/gardeners and workers in Group A on the risk of ESCC (Table 4). We found that the longer employment in Group A, the higher risk of ESCC. The similar result was not found in farmers/gardeners. The details of the multivariate logistic regression model are available upon request.

Table 1 Distribution of demographic characteristics among 326 esophageal cancer and 386 controls.

Variables	Cases	Controls	p value
Mean ± SD			
Age (y)	57.98 ± 11.55	56.79 ± 11.51	0.17
N (%)			
Educational level[a]			
Primary school	170 (52.2)	77 (20.0)	<0.0001
High school	122 (37.4)	127 (32.9)	
College	21 (6.4)	173 (44.8)	
Cigarette smoking			
No	27 (8.3)	198 (51.3)	<0.0001
Yes	299 (91.7)	188 (48.7)	
Alcohol drinking			
No	57 (17.5)	269 (69.7)	<0.0001
Yes	269 (82.5)	117 (30.1)	
Areca chewing			
No	146 (44.8)	350 (90.7)	<0.0001
Yes	180 (55.2)	36 (9.3)	

SD: standard deviation. Observations with missing data were excluded from the analyses.
[a] Missing data: 13 cases and 9 controls.

Table 2 Distribution of occupational variables among case patients and controls.

Occupations	Cases	Controls	p value
	N (%)	N (%)	
Farmers/gardeners			
No	280 (85.9)	365 (94.6)	<0.0001
Yes	46 (14.1)	21 (5.4)	
Group A (dust exposure)			
No	272 (83.4)	375 (97.2)	<0.0001
Yes	54 (16.6)	11 (2.8)	
Group B (metal exposure)			
No	299 (91.7)	380 (98.4)	<0.0001
Yes	27 (8.3)	6 (1.6)	
Petrochemical or plastic company workers			
No	322 (98.8)	380 (98.4)	0.76*
Yes	4 (1.2)	6 (1.6)	
Quarryman			
No	325 (99.7)	386 (100)	0.46*
Yes	1 (0.3)	0 (0)	
Leather maker			
No	325 (99.7)	385 (99.7)	1.00*
Yes	1 (0.3)	1 (0.3)	
Weaver			
No	325 (99.7)	386 (100)	0.46*
Yes	1 (0.3)	0 (0)	
Coking worker			
No	326 (100)	385 (99.7)	1.00*
Yes	0 (0)	1 (0.3)	
Hairdresser			
No	323 (99.1)	386 (100)	0.1*
Yes	3 (0.9)	0 (0)	
Paper-making worker			
No	325 (99.7)	385 (99.7)	1.00*
Yes	1 (0.3)	1 (0.3)	
Bird keeper			
No	325 (99.7)	386 (100)	0.46*
Yes	1 (0.3)	0 (0)	
Incense manufacturing worker			
No	325 (99.7)	386 (100)	0.46*
Yes	1 (0.3)	0 (0)	
Tobacco manufacturing worker			
No	326 (100)	385 (99.7)	1.00*
Yes	0 (0)	1 (0.3)	
Brewer			
No	325 (99.7)	385 (99.7)	1.00*
Yes	1 (0.3)	1 (0.3)	

Group A: concrete/construction, road construction and maintenance, carpenter, woodcutter and ship building or breaking workers.
Group B: automobile mechanics, iron/steel company, painter, and welders.
* Fisher exact test.

Table 3 Risk of occupations on esophageal squamous cell carcinoma in the multiple logistic models.

Occupations	Cases N (%)	Controls N (%)	OR (95% CI)	p value	AOR (95% CI)*	p value*
Farmers/gardeners						
No	280 (43.4)	365 (56.6)	1	<0.0001	1	0.04
Yes	46 (68.7)	21 (31.3)	2.86 (1.67—4.90)		2.08 (1.02—4.24)	
Group A (dust exposure)						
No	272 (42.0)	375 (58.0)	1	<0.0001	1	0.02
Yes	54 (83.1)	11 (16.9)	6.77 (3.47—13.18)		2.80 (1.21—6.47)	
Group B (metal exposure)						
No	299 (44.0)	380 (56.0)	1	<0.0001	1	0.41
Yes	27(81.8)	6 (18.2)	5.72 (2.33—14.03)		1.57 (0.54—6.61)	

Group A: concrete/construction, road construction and maintenance, carpenter and woodcutter, and shipbuilding or breaking workers.
Group B: automobile mechanics, Iron/steel company, painter and welders.
 * Adjusted for educational levels, cigarette smoking, alcohol drinking, and areca nut chewing.

Discussion

In this study, we found about two-fold increased risk among farmers and gardeners. Observational studies about cancer risks among agricultural workers were conducted a long time ago with paucity of update. Similar to our finding, farmer-workers were more prevalent among esophageal cancer patients in a highly prevalent area of Brazil [11]. Italian, but not Danish, male farmers were found to have a higher risk of esophageal cancer, and the effect of alcohol consumption could not be eliminated [12]. A large study in the United States revealed that nonwhite farm workers had a significant excess of mortality from esophageal cancer [13]. On the contrary, many studies reported similar or lower overall cancer risk among agricultural workers than general population [12,14—16]. This observation could possibly be attributable to "healthy worker effects" [14]. Lifestyles vary among farmers from different areas. Chao and colleagues [15] suggested that the lower esophageal cancer incidence among Swedish farmers might come from the healthier lifestyles and less alcohol and tobacco consumption. However, Italian farmers tended to have drinking habits and thus had higher esophageal cancer incidence while Danish workers did not [12].

The work environment in agriculture is complex, with many potential hazardous exposures, such as pesticides, herbicides, fertilizers, dusts, zoonotic microbes, and sunlight. The literature regarding cancer development among pesticide-exposed workers is limited and controversial. Jansson and colleagues [9] found a tendency of positive associations between high exposure to pesticides and risk of esophageal cancer (OR = 2.3, 95% CI = 0.9—5.7). A review study concluded little indication of increased cancer risk among pesticide manufacturers or sprayers [17]. However, the common limitations are small sample size, lack of exposure assessment, and the small number of studies. In addition to similar workplace exposures, farmers and farm workers are all labor-intensive jobs and they usually have lower socioeconomic status. Therefore, smoking, alcohol drinking, and lack of nutrients could also contribute to a higher esophageal cancer incidence among them.

We found workers who have dust exposure in the workplace had higher ESCC risk (AOR = 2.80, 95% CI = 1.21—6.47). In addition, the longer duration of employment in dust exposure, the higher risk of ESCC. Significantly increased ESCC risk has been reported among concrete and construction workers, which might be a result of exposure to inhaled particles [9,18]. In the construction

Table 4 Years of employment in particular occupations and the risk of esophageal squamous cell carcinoma.

Occupation	Duration of employment (y)	Cases N (%)	Control N (%)	OR (95%CI)	p value	AOR (95% CI)*	p value*
Farmers/gardeners							
No		280 (85.9)	365 (94.6)	1		1	
Yes[a]	1—33	21 (6.5)	7 (1.8)	3.91 (1.64—9.33)	0.06	4.19 (1.40—12.57)	0.01
	>33	20 (6.1)	7 (1.8)	3.72 (1.55—8.93)	0.08	2.19 (0.74—6.46)	0.16
	Missing	5 (1.5)	7 (1.8)	0.93 (0.29—2.97)	0.12	0.72 (0.17—2.97)	0.65
Group A (dust exposure)							
No		272 (83.4)	375 (97.2)	1		1	
Yes[a]	1—22	24 (7.4)	7 (1.8)	4.73 (2.01—11.13)	0.44	2.17 (0.79—5.97)	0.13
	>22	28 (8.6)	2 (0.5)	19.30 (4.56—81.68)	0.004	9.24 (1.35—63.37)	0.02
	Missing	2 (0.6)	2 (0.5)	1.38 (0.19—9.85)	0.26	0.90 (0.07—11.33)	0.93

*Adjusted for educational levels, cigarette smoking, alcohol drinking, and areca chewing.
 [a] Median year of employment in farmer/gardener: 33 years; Group A: 22 years.

industry, silica dust is an inhalation hazard, which has been reported to cause an increase in esophageal cancer risk [8,19,20]. It was speculated that sharp silica might cause repeated local injury or bury in the mucosa during their passage down the esophagus, providing anchorage and stimulating proliferation [21]. Wood dust has been known as a human carcinogen, leading to several health hazards, especially nasal adenocarcinoma [22]. However, few studies examined its association with esophageal cancer and did not find an excess risk in the relatively small subgroups with wood dust exposure [7,23]. Further studies are needed to clarify the role and carcinogenic effects of dust exposures on esophageal cancer.

The borderline significance for an increased ESCC risk among workers in Group B (exposure to welding fume and metals such as aluminum, iron, and lead) could be partially attributed to the relatively small sample size. It is also possible that those workers had more substance (cigarette, alcohol, and areca nut) consumption habits and the effect of occupational exposure could only be revealed when there were more participants. Siew and colleagues [24] reported that occupational exposure to iron and welding fumes was associated with an increase in lung cancer risk, mainly cell type of squamous-cell carcinoma. Parent and coauthors [7] did not find excess esophageal cancer risks among workers with metal exposure. However, they only recruited 99 esophageal cancer participants, 63 among whom had ESCC.

Previous studies have reported significant associations between other occupations and ESCC risk. For example, waiters/bartenders (OR = 8.18, 95% CI = 1.98–33.75) and miners/shot firers/stone cutters/carvers (OR = 10.78, 95% CI = 1.24–93.7) had higher ESCC risk in a Spanish study [25]. A borderline or significant trend of increased ESCC risk was also found in warehouse workers, food services workers, and workers from the miscellaneous food industry [7] as well as hotel and restaurant workers (OR=3.9, 95% CI=1.2–12.5) [9]. All those evidences suggest occupational exposure cannot be ignored in the study of esophageal cancer.

This study has several limitations. First, although the range of occupations was broad, the subjects collected for each occupation were relatively small, which could have biased our results. Second, most risk factors in this series were based on self-reported data and may be subject to recall bias. Third, the exposure intensity of specific occupation-related chemicals was not measured in this study. Further prospective cohort studies with detailed occupational information and exposure assessment are needed to elucidate how/what workplace hazards contribute to the development of esophageal cancers.

In conclusion, our results suggested that farmer/gardener and workers with exposure to dust were at higher risk to develop ESCC. Such association remained significant after adjusting for major risk factors of ESCC in Taiwan. This study added further evidence to the current knowledge that occupational hazards are important in the development of ESCC.

Acknowledgments

References

[1] Parkin DM, Bray F, Ferlay J, Pisani P. Global cancer statistics, 2002. CA Cancer J Clin 2005;55:74–108.

[2] Cancer Registry Annual Report. Taiwan, Republic of China: Published by Bureau of Health Promotion, Department of Health, The Execitive Yuan; 2007.

[3] Lee CH, Wu DC, Lee JM, Wu IC, Goan YG, Kao EL, et al. Carcinogenetic impact of alcohol intake on squamous cell carcinoma risk of the oesophagus in relation to tobacco smoking. Eur J Cancer 2007;43:1188–99.

[4] Lee CH, Lee JM, Wu DC, Hsu HK, Kao EL, Huang HL, et al. Independent and combined effects of alcohol intake, tobacco smoking and betel quid chewing on the risk of esophageal cancer in Taiwan. Int J Cancer 2005;113:475–82.

[5] Wu MT, Wu DC, Hsu HK, Kao EL, Lee JM. Relationship between site of oesophageal cancer and areca chewing and smoking in Taiwan. Br J Cancer 2003;89:1202–4.

[6] Gledovic Z, Grgurevic A, Pekmezovic T, Pantelic S, Kisic D. Risk factors for esophageal cancer in Serbia. Indian J Gastroenterol 2007;26:265–8.

[7] Parent ME, Siemiatycki J, Fritschi L. Workplace exposures and oesophageal cancer. Occup Environ Med 2000;57:325–34.

[8] Pan G, Takahashi K, Feng Y, Liu L, Liu T, Zhang S, et al. Nested case-control study of esophageal cancer in relation to occupational exposure to silica and other dusts. Am J Ind Med 1999;35:272–80.

[9] Jansson C, Plato N, Johansson AL, Nyren O, Lagergren J. Airborne occupational exposures and risk of oesophageal and cardia adenocarcinoma. Occup Environ Med 2006;63:107–12.

[10] Scarselli A, Binazzi A, Ferrante P, Marinaccio A. Occupational exposure levels to wood dust in Italy, 1996-2006. Occup Environ Med 2008;65:567–74.

[11] Dietz J, Pardo SH, Furtado CD, Harzheim E, Furtado AD. Risk factors related to esophageal cancer in Rio Grande do Sul, Brazil. Rev Assoc Med Bras 1998;44:269–72.

[12] Ronco G, Costa G, Lynge E. Cancer risk among Danish and Italian farmers. Br J Ind Med 1992;49:220–5.

[13] Colt JS, Stallones L, Cameron LL, Dosemeci M, Zahm SH. Proportionate mortality among US migrant and seasonal farmworkers in twenty-four states. Am J Ind Med 2001;40:604–11.

[14] Maroni M, Fait A. Health effects in man from long-term exposure to pesticides. A review of the 1975-1991 literature. Toxicology 1993;78:1–180.

[15] Chow WH, McLaughlin JK, Malker HS, Linet MS, Weiner JA, Stone BJ. Esophageal cancer and occupation in a cohort of Swedish men. Am J Ind Med 1995;27:749–57.

[16] Pearce N, Reif JS. Epidemiologic studies of cancer in agricultural workers. Am J Ind Med 1990;18:133–48.

[17] Burns CJ. Cancer among pesticide manufacturers and applicators. Scand J Work Environ Health 2005;31(Suppl. 1):9–17.

[18] Cucino C, Sonnenberg A. Occupational mortality from squamous cell carcinoma of the esophagus in the United States during 1991-1996. Dig Dis Sci 2002;47:568–72.

[19] Yu IT, Tse LA, Wong TW, Leung CC, Tam CM, Chan AC. Further evidence for a link between silica dust and esophageal cancer. Int J Cancer 2005;114:479–83.

[20] Tsuda T, Mino Y, Babazono A, Shigemi J, Otsu T, Yamamoto E. A case-control study of the relationships among silica exposure, gastric cancer, and esophageal cancer. Am J Ind Med 2001;39:52–7.

[21] O'Neill C, Pan Q, Clarke G, Liu F, Hodges G, Ge M, et al. Silica fragments from millet bran in mucosa surrounding oesophageal tumours in patients in northern China. Lancet 1982;1: 1202—6.

[22] d'Errico A, Pasian S, Baratti A, Zanelli R, Alfonzo S, Gilardi L, et al. A case-control study on occupational risk factors for sino-nasal cancer. Occup Environ Med 2009;66:448—55.

[23] Jansson C, Johansson AL, Bergdahl IA, Dickman PW, Plato N, Adami J, et al. Occupational exposures and risk of esophageal and gastric cardia cancers among male Swedish construction workers. Cancer Causes Control 2005;16:755—64.

[24] Siew SS, Kauppinen T, Kyyronen P, Heikkila P, Pukkala E. Exposure to iron and welding fumes and the risk of lung cancer. Scand J Work Environ Health 2008;34:444—50.

[25] Santibanez M, Vioque J, Alguacil J, Barber X, Garcia de la Hera M, Kauppinen T. Occupational exposures and risk of oesophageal cancer by histological type: a case-control study in eastern Spain. Occup Environ Med 2008;65:774—81.