Tobacco, alcohol intake, and diet in relation to adenocarcinoma of the esophagus and gastric cardia

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Little is known about the etiology of adenocarcinoma of the distal esophagus/cardia, a cancer which has increased in incidence in the United States over the last two decades. We analyzed data on smoking, alcohol use, dietary intake, and other factors obtained from 173 hospitalized males with adenocarcinoma of the distal esophagus/cardia (cases) and 4,544 hospitalized males with diseases not related to smoking and of other organ systems than the gastrointestinal tract (controls). Cases of squamous cell carcinoma of the esophagus (n = 136) and adenocarcinoma of the distal stomach (n = 122) were included as separate case groups. All subjects were interviewed in 28 hospitals in eight cities in the US between 1981 and 1990. After adjustment for covariates, the odds ratio (OR) for adenocarcinoma of the distal esophagus/cardia for current smokers was 2.3 (95 percent confidence interval [CI] = 1.4-3.9) and that for ex-smokers was 1.9 (CI = 1.2-3.0) relative to never-smokers. The OR for drinkers of four or more ounces of whiskey-equivalents of alcohol per day (relative to those consuming less than one drink per week) was 2.3 (CI = 1.3-4.3). Intakes of total fat and vitamin A from animal sources were significant risk factors and fiber intake was associated inversely with adenocarcinoma of the distal esophagus/cardia. Although the number of female cases of adenocarcinoma of the distal esophagus/cardia was small (n = 21), significant associations were observed for smoking and alcohol.

Key words: Alcohol, body mass index, dietary factors, esophageal cancer, gastric cancer, smoking, United States.

Introduction

The age-adjusted incidence of adenocarcinoma of the distal esophagus and cardia has been increasing steadily in the United States since at least the mid-1970s in contrast to the incidence of squamous cell carcinoma of the esophagus, which has been stable. An increase in the incidence of adenocarcinoma of the distal esophagus and cardia has been noted also in the United Kingdom and Denmark. Although the number of female cases of adenocarcinoma of the distal esophagus and cardia was small (n = 21), significant associations were observed for smoking and alcohol.

Key words: Alcohol, body mass index, dietary factors, esophageal cancer, gastric cancer, smoking, United States.
In addition, several case-control studies have examined risk factors for adenocarcinoma of the esophagus and/or gastric cardia.\textsuperscript{12-16}

Using data from a hospital-based case-control study of tobacco-related cancers carried out between 1981 and 1990,\textsuperscript{17} we analyzed data on smoking, alcohol, diet, and other risk factors in relation to: (i) squamous cell carcinoma of the esophagus; (ii) adenocarcinoma of the distal esophagus, gastro-esophageal junction, or cardia; and (iii) adenocarcinoma of the distal stomach.

**Materials and methods**

In the original study, newly diagnosed, histologically confirmed, primary cases of tobacco-related cancers (lung, larynx, oral cavity, bladder, kidney, pancreas and squamous cell carcinoma of the esophagus) were interviewed in 28 hospitals in eight US cities (NYC, NY; Birmingham, AL; Chicago, IL; Detroit, MI; Philadelphia, PA; Pittsburgh, PA; San Francisco, CA; Atlanta, GA).\textsuperscript{17} For each case, a control patient with an admitting diagnosis of a condition not known to be associated with tobacco use was selected and interviewed within two months of the case interview. Controls were matched to cases on age (± 5 years), sex, race, and hospital. Control diagnoses included non-tobacco related cancers (stomach; colorectum; breast; prostate; endometrium; ovary; leukemia; lymphoma; sarcomas; central nervous system tumors, etc.), as well as non-cancer diagnoses (acute infections; fractures; spinal disc problems; other trauma; arthritis; and ophthalmological conditions).

Adenocarcinoma of the esophagus or cardia were both acceptable controls according to the study protocol and were coded as "stomach cancer". For the purposes of the present analysis, all diagnoses of both esophageal (among cases and controls) and stomach cancer (among controls) were reviewed and reclassified, using information recorded by the interviewer on the face sheet of the questionnaire—which included subsite and cell type—into three groups, according to the International Classification of Diseases, Ninth Revision\textsuperscript{18} (ICD-9): (i) squamous cell carcinoma of the esophagus (ICD-9 code 150); (ii) adenocarcinoma of the distal esophagus, gastro-esophageal junction, or cardia (151.0); and (iii) adenocarcinoma of the distal stomach (151.1-151.9).

No attempt was made to separate adenocarcinoma of the distal esophagus or gastro-esophageal junction from adenocarcinoma of the cardia. The majority of cases had "gastro-esophageal junction" as the specified subsite, and we henceforth will refer globally to adenocarcinoma of the esophagus/cardia (AEC). Out of 587 cancers of the esophagus or stomach, 26 (4.4 percent) were excluded for the following reasons: uncertain cell type or subsite (n = 9); non-carcinomas (carcinoid, lymphoma, leiomyosarcoma) (n = 15); adenocarcinoma located in the middle third of the esophagus (n = 2).

For the present analysis, all digestive tract cancers (mainly of the colon and rectum) were excluded from the control group. The distribution of the remaining diagnoses among the controls was as follows: in males, 38 percent cancers (including, in declining order of frequency, prostate, skin, lymphoma, sarcoma, and leukemia) and 62 percent non-cancers (including fractures, disc problems, trauma, hernias, benign prostatic hypertrophy, eye problems, and acute infections); in females, 54 percent cancers (breast, ovary, endometrium, skin, leukemia, lymphoma, and sarcoma) and 46 percent non-cancers (including arthritis, fractures, disc problems, eye problems, acute infections and trauma).

Since there was only a small number of non-White cases, the analysis was limited to Whites.

All subjects were interviewed in the hospital by trained interviewers using a questionnaire covering the following content areas: demographics; occupation and occupational exposures; detailed smoking history; alcohol use; medical history; vitamin and mineral supplements; height; and weight five years prior to diagnosis.

For the period 1985-90, a brief food-frequency questionnaire including 30 specific food items or classes of foods was used, as previously described.\textsuperscript{19} These foods were judged to account for approximately 80 percent of the average American intake of dietary fat and vitamin A from plant and animal sources. Subjects were asked for their usual adult intake prior to the onset of the current illness. Portion sizes were not asked, except in the case of eggs and milk. For the remaining foods, a standard portion size was assigned to each food item. Nutrient scores other than fiber were computed using the USDA's food composition tables.\textsuperscript{20} Fiber values were taken from Anderson.\textsuperscript{21} Computation of nutrient scores involved summing, for each subject, the amount of each nutrient derived from each of the food items contributing to that nutrient. The sex-specific quartile distributions of the dietary scores and of body mass index (BMI, weight [kg]/height [m]\textsuperscript{2}) were used to compute odds ratios (OR). The percentage of total subjects interviewed between 1985 and 1990 and on whom we had dietary data was 50 percent in males and 53 percent in females. For AEC cases, however, the percentage was higher (77 percent in males and 76 percent in females due to the increasing frequency of this cancer over the study period (Figure 1).