Demographic and Lifestyle Predictors of Survival in Patients With Esophageal or Gastric Cancers

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Background & Aims: **Risk factors for subtypes of esophageal and gastric cancer recently have been identified, but their effect on survival is unknown.** ***Methods:*** **Incident cases (n = 1142) from a population-based case-control study were followed-up from diagnosis (1993–1995) until 2000. Cox regression models were used to estimate adjusted hazard ratios (HRs) and 95% confidence intervals (CIs) for esophageal and gastric cancer in relation to prediagnostic factors.** ***Results:*** **Relative to distant stage, esophageal adenocarcinoma (EA) patients with localized disease had a decreased risk for death (HR, .22; 95% CI, .15–.31), followed by those with regional spread (HR, .32; 95% CI, .23–.45). Similar patterns were seen for the other tumor types. Except for other (non-cardia) gastric adenocarcinomas (OGA), higher household income (≥$15,000/y vs. <$15,000/y) was associated with a 33%–38% decrease in risk for death. Prediagnosis body mass index (BMI) between 25 and 29.9 kg/m² was associated with longer survival for EA and OGA patients (EA: HR, .67; 95% CI, .51–.88) vs. BMI <25 kg/m². Women with esophageal squamous cell carcinoma (ES) and OGA experienced longer survival compared with men. Age, education, cigarette smoking, alcohol intake, gastroesophageal reflux disease, and nonsteroidal anti-inflammatory drug use did not consistently predict survival.** ***Conclusions:*** **Predictors of lengthened esophageal and gastric cancer survival included higher income (except in OGA), overweight (among EA and OGA patients), and female sex (among ES and OGA patients).**

Worldwide, gastric cancer is the second leading cause of cancer mortality.[1] Gastric cancer incidence is relatively low in the United States, but the burden is substantial, with 22,700 cases and 11,780 deaths estimated to occur in 2004.[2] Esophageal cancer is more lethal, with 14,250 cases and 13,300 deaths expected in 2004.[2] Tumor-specific risk factors have been identified including cigarette smoking, alcohol consumption, high body mass index (BMI), diet, *Helicobacter pylori* infection, gastroesophageal reflux disease, and limited use of nonsteroidal anti-inflammatory drugs.[3–8] Predictors of survival are not well characterized. Prognosis is poor, with 5-year relative survival rates between 15% and 21% for esophageal and gastric tumors, respectively.[2] Previous survival studies have focused on gastric cancer, indicating the importance of stage, grade, surgical treatment, and sex, whereas inconsistent results have been observed for race, education, and income.[9–16] Increased BMI and gastroesophageal reflux disease, risk factors for esophageal and gastric cardia adenocarcinoma,[4,8] have not been studied in relation to survival.

We sought to determine whether prediagnostic demographic, lifestyle, and anthropometric risk factors have prognostic significance for any of the tumor types.

Materials and Methods

Study Population

Patients were identified as part of a multicenter, population-based, case-control study of esophageal and gastric cancer. The study details have been described previously.[5] Incident invasive cases of esophageal adenocarcinoma (EA), gastric cardia adenocarcinoma, esophageal squamous cell carcinoma (ES), or other (non-cardia) gastric adenocarcinomas

Abbreviations used in this paper: EA, esophageal adenocarcinoma; ES, esophageal squamous cell carcinoma; OGA, other (non-cardia) gastric adenocarcinomas; HR, hazard ratio; CI, confidence interval; BMI, body mass index.

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(OGA), aged 30–79 years, and diagnosed between 1993 and 1995, were ascertained using rapid reporting systems in Connecticut, New Jersey, and western Washington state. Final case eligibility and tumor type was determined by 2 authors (H.R., A.B.W.) through standardized pathology review. Baseline interviews were completed for 80.6% of EA (n = 293) and gastric cardia adenocarcinoma (n = 261) patients, and 74.1% of ES (n = 221) and OGA (n = 367) patients.

Vital status and date of death were determined through the National Death Index, with maximum follow-up of 90 months. Survival time (in months) was calculated from the date of diagnosis through the date of death or last follow-up. A failure was defined as death from any cause during the follow-up period and patients alive at the end of the follow-up period were censored. Three patients were excluded from all analyses (2 patients lost to follow-up, 1 patient owing to a discrepancy between the date of diagnosis and death). Follow-up ceased in Washington state in July 2000, in New Jersey on September 15, 2000, and in Connecticut on October 28, 2000. All appropriate Institutional Review Boards approved this study.

Statistical Methods

Kaplan–Meier plots were used to determine univariate predictors of survival, and Cox proportional hazard regression analysis was used to build multivariable models and estimate hazard ratios (HRs; risk for death) and 95% confidence intervals (CIs). Separate models were run for each tumor type in relation to tumor characteristics assessed by medical record (Surveillance, Epidemiology, and End-Results program [http://seer.cancer.gov] summary stage, histologic grade) and prediagnostic lifestyle/demographic characteristics obtained from the respondent (within approximately 3 months of diagnosis), or a proxy (within approximately 8.5 months of diagnosis) (usual adult BMI, frequency of gastroesophageal reflux disease symptoms, and over-the-counter and prescription nonsteroidal anti-inflammatory drug use, household income, education, and tobacco and alcohol consumption). All were entered as dichotomous or indicator variables by using similar categories as in previous reports[5,8] except for BMI, which was categorized by using World Health Organization recommendations (overweight, $\geq$25 kg/m^2; obese, $\geq$30 kg/m^2).[17]

Multivariable HR models were constructed by using backward selection, and included variables that statistically significantly predicted survival or confounded another characteristic already present in the model. Referent groups were chosen so the majority of HR estimates would be less than 1. Results were not materially different when excluding proxy respondents (n = 355, 31%) or those with imputed income information (10%).

The potential confounding effect of cancer-directed surgery within 4 months of diagnosis as recorded by the Surveillance, Epidemiology, and End-Results program also was evaluated. In models based only among individuals with complete treatment data (n = 610), adjustment for surgery did not materially change any estimates. Thus, surgery was not included in the models shown. Race (for ES and OGA only) was considered as a confounder, but did not alter any estimates.

No violations of the proportional hazards assumption were observed. Absolute differences in survival were calculated by comparing modeled (adjusted) median survival times across strata of covariates, which were evaluated at the reference level of all other variables in the model. Statistical significance was noted when the 2-sided P value was $< .05$.

Results

The majority of patients had regional or distant disease. Most patients completed high school, but made less than $30,000 per year (Table 1). The percentage of patients alive at the end of 7.5 years of follow-up ranged from 12% for ES to 20% for OGA (Table 1). Median survival times were 9.6 months (95% CI, 8.4–10.9 mo), 10.7 (95% CI, 8.9–12.6 mo), 12.8 (95% CI, 10.2–15.3 mo), and 12.9 (95% CI, 10.6–15.2 mo) for EA, ES, gastric cardia adenocarcinoma, and OGA, respectively.

In unadjusted models for all considered variables (Table 2), predictors of lengthened survival included low stage (for all tumor types), increased BMI (in EA and OGA patients), and household income greater than $15,000 per year (except in OGA). Table 3 highlights important predictors remaining after multivariable modeling. For all tumor subtypes, stage was the most important predictor of survival, with patients having lower-staged tumors experiencing a decreased risk for death relative to distant stage. Adjusted HRs for EA were .22 (95% CI, .15–.31) for localized and .32 (95% CI, .23–.45) for regional tumors. Estimates were similar for other tumor types, with decreased risks for death ranging from 60% to 88% for localized tumors, and from 51% to 65% for regional tumors.

Relative to households making less than $15,000 per year, higher income was associated with a 33%–38% decreased risk for death, except among OGA patients. When income was evaluated using multilevel variables, little variation in survival existed for categories greater than $15,000 and race did not confound the relationship (results not shown). In addition, women with ES and OGA had longer survival than men, with adjusted HRs of .57 (95% CI, .39–.83) and .77 (95% CI, .60–1.00), respectively.

Survival was most favorable in overweight EA and OGA patients (based on usual prediagnosis adult weight) relative to normal and underweight or obese patients (Table 3). Adjusted HRs for EA were .67 (95% CI, .51–.88) and .78 (95% CI, .55–1.12) for overweight and obese patients, respectively. Similar results were observed for overweight OGA patients. Alcohol drinking and cigarette smoking did not confound these relationships.