Clinical Science

The role of diabetes and other co-morbidities on survival after esophageal cancer surgery in a population-based study

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KEYWORDS:
Prospective;
Esophagectomy;
Esophageal resection;
Postoperative;
Cardia

Abstract
   BACKGROUND: There is limited knowledge on how diabetes and other comorbidities influence the survival of patients undergoing curative esophageal cancer surgery.
   METHODS: A population-based and prospective cohort study included patients who underwent surgical resection for esophageal or cardia cancer in Sweden from 2001 to 2005, with follow-up until 2011. Associations between diabetes and other comorbidities in relation to postoperative mortality were analyzed using Cox proportional-hazards regression with adjustment for potential confounding factors.
   RESULTS: Among 609 patients, 67 (11%) with diabetes had no increased risk for mortality compared with those without diabetes (hazard ratio, .81; 95% confidence interval, .60 to 1.09). Compared with patients without any predefined comorbidities, those with 1 (hazard ratio, 1.15; 95% confidence interval, .93 to 1.43) or ≥2 comorbidities (hazard ratio, 1.05; 95% confidence interval, .83 to 1.33) had no statistically significantly increased risk for mortality.
   CONCLUSIONS: This study revealed no strongly increased risk for mortality in patients with diabetes or other comorbidities selected for esophageal cancer surgery.
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Esophageal cancer is the 8th most common cancer and the 6th most common cause of cancer death worldwide.[1] The overall survival rate at 5 years is only 10% to 15% in Western populations.[1,2] Esophageal resection is the major established treatment with curative intent, resulting in a population-based 5-year survival of 30%.[3,4] About 65% to 80% of all patients with esophageal cancer are considered ineligible for surgery in Western populations.[4,5] For those with local disease alone, the main reason for exclusion from surgery is poor performance status, which is often due to comorbidities.[4–6] However, the exclusion of patients with comorbidities is supported by scientific evidence to only a limited degree.[5] Some studies indicate that diabetes might be of particular relevance for prognosis after esophageal cancer surgery,[7–9] but more research is needed to enable

evidence-based clinical decision making. Type 2 diabetes mellitus is the most common chronic metabolic disease, with a global prevalence of 366 million people, which is expected to rise to 552 million by 2030.[10] The increasing number of patients with diabetes stresses the relevance of clarifying the role of diabetes in the prognosis after esophageal cancer surgery. We conducted a population-based cohort study to test the hypothesis that patients with esophageal cancer with diabetes and other predefined comorbidities experience a worse prognosis after esophageal cancer resection than those without comorbidities.

Methods

Study design

This was a nationwide, Swedish, population-based prospective cohort study of patients diagnosed with esophageal or esophagogastric junctional cancer who underwent curative esophageal resection from April 2, 2001, to December 31, 2005, with follow-up until death or the end of the study period (May 31, 2011). Informed consent was obtained from all participating patients, and the Regional Ethical Review Board in Stockholm, Sweden, approved the study.

Data collection

Data were collected from the prospective Swedish Esophageal and Cardia Cancer Database, which has been described in detail elsewhere.[11,12] In brief, 174 of 179 hospitals (97%) participated in data collection. Nonparticipation (10%) was attributed mainly to 5 centers that did not participate. Data collection began with a histopathology report confirming esophageal or esophagogastric junctional cancer and continued by contacting the relevant hospital departments and physicians involved in the staging of the tumor or treatment of the patient. Data regarding comorbidities, tumor characteristics, preoperative physical examination, surgical treatment, and complications were prospectively collected on the basis of a predefined study protocol, developed by experienced esophageal surgeons and epidemiologists.

Study exposures: comorbidities

The main comorbidity being evaluated was diabetes (yes or no). This was further combined with the following groups of other commonly occurring comorbidities: (1) cardiovascular disease; (2) hypertension; (3) pulmonary disease; and (4) any other predefined comorbidity. Other predefined comorbidities were cardiovascular disease (angina and heart failure), hypertension, pulmonary disease (chronic obstructive pulmonary disease and asthma), and other (liver failure, renal failure, nonesophageal cancer, or any other significant disease defined by experienced physicians while manually reviewing medical charts). In addition, patients were classified as having no, 1, or ≥2 comorbidities.

Study outcome: mortality

Patients were followed through linkage to the Swedish Registry of the Total Population, which includes complete information about the vital status of all Swedish residents. This linkage was made possible by the personal identity number, a 10-digit number unique for each Swedish resident.[13]

Statistical analysis

Baseline characteristics among patients with and without diabetes and other comorbidities were compared using chi-square tests, and survival curves were drawn using the Kaplan-Meier method. To determine the risk for mortality in patients with and without diabetes and other comorbidities, a multivariate Cox proportional-hazards regression model was used to provide adjusted hazard ratios (HRs) with 95% confidence intervals (CIs). The potential confounding factors included in the model were age (categorized into 3 groups: <60, 60 to 74, or ≥75 years), sex, tumor stage (0 and I, II, or III and IV), tumor histology (adenocarcinoma or squamous cell carcinoma), type of surgery (esophageal resection, cardia resection, extended total gastrectomy, or total gastrectomy and esophageal resection), number of postoperative complications (0, 1, or ≥2), and other comorbidities. Postoperative complications included the following predefined complications: postoperative bleeding <2 L, leakage or perforation of the anastomosis, stricture of the anastomosis, wound infection requiring intervention, wound rupture, gastric perforation, intra-abdominal or intrathoracic abscess, septicaemia, ileus, thoracic duct injury, renal failure, reintubation or need for prolonged mechanical ventilation, progressive jaundice, paresis of the recurrent laryngeal nerve, pneumonia, pulmonary thrombosis, deep vein thrombosis, myocardial infarction, atrial fibrillation, stroke, or other specified complication. Other comorbidities included cardiac disease, hypertension, diabetes, pulmonary disease, liver failure, renal failure, nonesophageal cancer, or any significant disease other than the one being analyzed for. All statistical analyses were completed using Stata version 12 for Windows (StataCorp LP, College Station, TX).

Results

Patient characteristics

A total of 616 patients were included in the database, representing 90% of all eligible patients in the study base. Because of missing data on tumor stage in 6 patients and missing histology in 1 patient, the final analyses were performed on 609 patients (99%). Characteristics of