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University hospital status and prognosis following surgery for esophageal cancer

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Abstract

Background: We hypothesized that such prognosis is independently improved by surgery conducted within university hospitals.

Methods: Patients undergoing esophagectomy for esophageal cancer between 1987 and 2010 with follow-up until 2014 were identified from population-based nationwide Swedish cohort study. The association between university hospital status in and mortality was analyzed using a multivariable Cox-proportional hazards model, providing hazard ratios (HRs) with 95% confidence intervals (CIs). The HRs were adjusted for surgeon volume as well as age, comorbidity, tumor stage, histological subtype, neoadjuvant therapy and calendar period.

Results: Among 1820 included patients, 989 (54.3%) had surgery at one of the six university hospitals. Of the 83 and 569 patients operated on by the higher surgeon volume (17–46 cases) and middle surgeon volume groups (7–16 cases), 60 (72.3%) and 430 cases (75.6%) respectively were performed within university hospitals. University hospitals status indicated a non-significant reduction in all-cause 90-day mortality (HR = 0.82, 95% CI 0.61–1.10), but all-cause 5-year (HR = 0.94, 95% CI 0.83–1.05) and disease-specific 5-year mortality (HR = 1.00, 95% CI 0.88–1.14) were similar to non-university hospitals. Higher surgeon volume (17–46 cases), showed non-significant reductions in all-cause 90-day (HR = 0.49, 95% CI 0.21–1.14), all-cause 5-year (HR = 0.80, 95% CI 0.61–1.06) and disease-specific 5-year mortality (HR = 0.81, 95% CI 0.60–1.09).

Conclusions: This study found no improvements in long-term mortality from esophagectomy performed within university hospitals after adjustment for surgeon volume and other confounders.

Keywords: Esophageal cancer; Esophagectomy; Mortality; University; Survival

Introduction

In recent years there has been steady improvement in short-term mortality following esophagectomy for esophageal cancer.[1–3] The reasons for this improvement are multi-factorial, but include[4–6] centralization of esophageal cancer services to high volume centers with the appropriate infrastructure to manage these complex patients and deliver a consistently high level of care.[7,8] However hospital volume appears to be less important when compared with surgeon volume, and may not be an independent long-term prognostic factor after adjusting for surgeon volume.[9,10] University hospitals traditionally have greater staffing levels, and with an academic climate enhancing critical review of service provision to continuously improve outcomes from surgery. Furthermore university hospitals more commonly conduct clinical trials, potentially allowing their patients to benefit from closer monitoring of postoperative outcomes with relevant interventions when needed, as well as innovative treatments that may complement surgery for esophageal cancer. The effect of university or academic hospital status has been evaluated only to a limited extend in other types of surgery and with a focus on short-term mortality.[11]

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The hypothesis under investigation was that the prognosis after esophageal cancer surgery is improved by surgery conducted within university hospitals even after adjusting for surgeon volume.

Methods

Study design

The design of this population-based cohort study has been described in detail elsewhere.[12] In brief, this Swedish nationwide cohort study included 98% of all patients with esophageal cancer treated with curative intended surgery between 1987 and 2010 with follow-up until November 2014. From the Swedish Cancer Registry, patients with a diagnosis of esophageal cancer (150.0, 150.8, or 150.9) were identified according to the 7th edition of the International Classification of Diseases (ICD7). This Cancer Registry has 98% nationwide coverage of esophageal cancer.[13,14] Esophageal cancer patients who underwent esophagectomy were identified from the Swedish Patient Registry, which has an excellent positive identification rate (99.6%) for esophageal cancer surgery.[15] The Patient Registry also provided data pertaining to patient medical comorbidities.[15] The comorbidities were classified according to the well-validated Charlson comorbidity index, and the esophageal cancer diagnosis was not counted.[16] The Swedish Causes of Death Registry provided accurate data for date and causes of death. This Registry has 100% coverage. If the diagnosis esophageal cancer was listed as a cause of death, this mortality was defined as disease-specific. The Swedish personal identity number, assigned to each Swedish resident at birth or immigration, was used to link individuals' data between registries and to identify their medical records. The clinical data collection was facilitated by a nationwide Swedish clinical network established in the mid-1990s.[17] Medical records containing operation notes and histopathology reports of the cohort members were retrieved from all Swedish hospitals where esophageal cancer surgery was performed during the entire study period. Data concerning operating hospital, names of the surgeons, neoadjuvant therapy, surgical therapy, pathological tumor stage and histological type were obtained from these individual patient records. The histopathological review has been demonstrated for its high accuracy.[18] Neoadjuvant therapy was predominantly used in more recent years, and when used was typically a combination of chemotherapy and radiotherapy. Tumor stage was classified according to the sixth edition TNM classification of the Union Internationale Contre le Cancer (UICC).[19] Open transthoracic esophageal resection with intrathoracic anastomosis was the dominating surgical procedure (95%). Patients transferred between hospitals for the management of complications were analyzed based upon the hospital where the primary esophagectomy was performed. The Regional Ethical Review Board in Stockholm, Sweden approved the study.

Exposures, outcomes and covariates

The exposure tested was surgery performed in any of the six Swedish university hospitals. The outcomes were all-cause 90-day and 5-year mortality as well as disease-specific 5-year mortality. Covariates considered as potential confounding factors were age (continuous variable), sex (male or female) pathological TNM tumor stage (0, I, II, III, or IV), Charlson comorbidity index (0, I, or ≥I), neoadjuvant therapy (yes or no), histological tumor type (adenocarcinoma or squamous cell carcinoma), cumulative surgeon volume of esophagectomies during study period (based upon previously validated tertile thresholds; ≤6, 7–16 or 17–46),[9] and calendar period (1987–1994, 1995–2002, or 2003–2010).

Statistical analysis

Kaplan-Meier survival analysis was conducted to visualize crude all-cause and disease-specific mortality within 5 years of surgery. University hospital status was analyzed in relation to mortality using a multivariable Cox-proportional hazards model, providing hazard ratios (HRs) with 95% confidence intervals (CIs), adjusted for eight potential confounding factors with categorizations as described above. These factors were included in the multivariable model because of their known prognostic influence. Two regression models were created one with (a) and one without (b) surgeon volume. The patients who underwent surgery within university hospitals were compared with patients who underwent surgery at non-university hospitals. To manage missing data (0.8%), a complete case analysis was carried out. Follow-up ended at the date of death or end of study period, whichever occurred first. The statistical software SPSS 23.0 (Statistical Package for the Social Sciences software, SPSS Chicago (IL), USA) was used for the data management and statistical analysis.

Results

Patients

The study included 1820 patients who underwent surgery for esophageal cancer. Characteristics of these patients are presented in Table 1. The average age was 65.1 years, with the majority of patients (58.5%) having a Charlson comorbidity index of 0. The incidences of 90-day all-cause, 5-year all-cause and 5-year disease-specific mortality were 11.4% (208/1820), 74.7% (1360/1820) and 79.7% (1197/1501), respectively. Within the dataset 989 patients (54.3%) had surgery within a university hospital. Comparison of patient demographics between university and non-university hospital groups showed a greater percentage