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ScienceDirect

EJSO 43 (2017) 1559–1565

EJSO the Journal of Cancer Surgery

www.ejso.com

The impact of pre- and post-operative weight loss and body mass index on prognosis in patients with oesophageal cancer

O. Hynes [a,b], P. Anandavadivelan [c], J. Gossage [a,b], A.M. Johar [c], J. Lagergren [a,b,d], P. Lagergren [c,*]

[a] Guy's and St. Thomas' NHS Foundation Trust, Westminster Bridge Road, London, SE1 7EH, United Kingdom
[b] Division of Cancer Studies, King's College London, Room 2.20A, New Hunt's House, Guy's Campus, London, SE1 1UL, United Kingdom
[c] Surgical Care Science, Department of Molecular Medicine and Surgery, Karolinska Institutet, Karolinska University Hospital, 17176 Stockholm, Sweden
[d] Upper Gastrointestinal Surgery, Department of Molecular Medicine and Surgery, Karolinska Institutet, Karolinska University Hospital, 17176 Stockholm, Sweden

Accepted 29 May 2017
Available online 15 June 2017

Abstract

Background: Weight loss is a cardinal symptom of oesophageal cancer and is often continued after surgery. High body mass index (BMI) is a strong risk factor for oesophageal adenocarcinoma. This study aimed to assess the impact of pre- and post-operative weight loss and BMI on long-term mortality after resection for oesophageal cancer.

Methods: This prospective and nationwide cohort study included 390 patients, operated on for oesophageal cancer in Sweden in 2001–2005 with follow-up until 2016, who responded to a questionnaire on weight history 6 months after surgery. Multivariable Cox proportional hazard models provided hazard ratios (HRs) and 95% confidence intervals (95% CIs) of mortality while adjusting for several prognostic factors, including tumour stage.

Results: Compared to weight stable patients, pre-surgery weight loss indicated increased HRs of overall all-cause mortality (HR = 1.32, 95% CI 0.94–1.86) and disease-specific mortality (HR = 1.36, 95% CI 0.93–1.98). Patients with >20% weight loss post-surgery had worse overall all-cause mortality (HR = 1.71, 95% CI 1.01–2.88) and disease-specific mortality (HR = 2.20, 95% CI 1.24–3.89). Compared to patients with normal BMI, decreased HRs were indicated for patients who were obese at the time of surgery (overall all-cause mortality HR 0.87 95% CI, 0.58–1.31 and disease-specific mortality HR = 0.89, 95% CI 0.57–1.40), while patients with BMI ≤19.9 at 6 months post-surgery had increased all-cause mortality (HR = 1.41, 95% CI 1.03–1.95) and disease-specific mortality (HR = 1.55, 95% CI 1.09–2.21).

Conclusion: Post-operative weight loss and low BMI at 6 months post-surgery are independent markers of poor prognosis in patients who undergo surgery for oesophageal cancer.

Keywords: Oesophageal neoplasm; Weight change; BMI; Survival; Mortality

Introduction

Oesophageal carcinoma is the sixth leading cause of cancer-related mortality and the eighth most common cancer worldwide.[1] The overall 5-year survival rates are poor (<20%)[2] and the incidence of adenocarcinoma of the oesophagus is increasing rapidly.[3] High body mass index (BMI) is a well-recognised risk factor for adenocarcinoma

* Corresponding author. Department of Molecular Medicine and Surgery, Norra Stationsgatan 67, level 2, Karolinska Institutet, SE-171 76 Stockholm, Sweden.
E-mail addresses: Orla.Hynes@gstt.nhs.uk (O. Hynes), poorna.anandavadivelan@ki.se (P. Anandavadivelan), jgossage@doctors.org.uk (J. Gossage), asif.johar@ki.se (A.M. Johar), Jesper.Lagergren@ki.se (J. Lagergren), Pernilla.Lagergren@ki.se (P. Lagergren).

http://dx.doi.org/10.1016/j.ejso.2017.05.023

of the oesophagus.[4,5] Weight loss is a common (57–83%) presenting symptom of oesophageal cancer.[6,7] Dysphagia, reduced oral intake, and altered nutrient metabolism associated with systemic inflammation induced by the tumour, can all contribute to this weight loss and malnutrition.[6–8] Surgery is the mainstay of curative treatment for patients diagnosed with locally advanced oesophageal cancer.[9] Malnutrition is associated with increased post-operative morbidity and mortality after gastrointestinal surgery.[10–12] Some research indicates that pre-operative weight loss of >10% is associated with reduced overall 5-year survival after surgery for oesophageal cancer.[13] Continued weight loss and malnutrition are also common after surgery; post-surgery weight loss is seen in most patients, and is often profound and long-lasting.[14,15] However, the impact of post-surgery weight loss on long-term survival has not been explored. The aim of this study was to assess the impact of pre- and post-operative weight loss and BMI on long-term survival after resection for oesophageal cancer.

Patients and methods

Design

This was a prospective nationwide cohort study in Sweden, which builds on a long-lasting and all-encompassing research network of hospital departments and clinicians with an interest in oesophageal cancer established in the 1990s.[16] During the period 2001–2005, 90% of all surgically treated patients with oesophageal cancer in Sweden were included and the participants were followed up regularly post-operatively until February 2016. The principles and organisation of the nationwide data collection have been described elsewhere. The ethics committee at the Karolinska University Hospital, Karolinska Institutet, Sweden, approved the study; reference numbers: 01-064, date: 2001-02-05; 01-340, date: 2005-12-29; 05/1491-32, date: 2005-12-29. Data regarding patient and tumour characteristics, hospital stay, surgery and complications were collected prospectively through continuous manual scrutiny of medical records. An extensive study protocol was completed by the study researchers for each patient, ensuring uniformity. Tumour stage was classified according to the International Union Against Cancer.[17] Mortality was determined by linkage to the 100% complete Swedish Register of the Total Population.[18] Data on weight changes were collected through written study-specific questionnaires assessing height and average weight as adults, weight just before operation, and weight at 6 months after surgery.[15] Patients who responded to this questionnaire were eligible for this study.

Exposures

The study exposures were weight changes and BMI at defined time points in relation to surgery. Weight changes were evaluated in three categories: 1) between the average weight as an adult and weight at time of operation ('Pre-operative weight change'); 2) between the time of surgery and 6 months following surgery ('Post-operative weight change'); and 3) between the average weight as an adult and weight at 6 months after surgery ('Pre-operative to post-operative weight change'). Weight changes were categorised into four groups: 1) Weight gain or stable weight (+/−1.0%); 2) 1.1–10.0% weight loss; 3) 10.1–20.0% weight loss; and 4) >20.0% weight loss. BMI (body weight in kilograms (kg) divided by the square of the body height in metres (m) [kg/m^2]) was assessed at two time points: 1) at operation and 2) at 6 months post-surgery. BMI was categorised into four groups: ≤19.9 ('low'), 2) 20.0–24.9 ('normal'), 3) 25.0–29.9 ('overweight'), and 4) ≥30.0 ('obesity').

Outcomes

All-cause and disease-specific mortality was measured in days after surgery and assessed as 6 months to end of study period (February 2016) and 6 months to 5 years. The follow-up from 6 months was because patients had to have survived for at least 6 months after their surgery to respond to the weight history questionnaires. All-cause mortality was defined as death from any cause during follow-up in the Swedish Causes of Death Registry.[18] Disease-specific mortality was defined as a death where oesophageal cancer was recorded as a cause of death during follow-up in the Causes of Death Registry.[18]

Statistical analysis

Kaplan Meyer survival curves were plotted and compared with the log rank test. Cox proportional hazard models were calculated to assess the hazard ratios (HRs) and 95% confidence intervals (CIs) of mortality associated with weight change and BMI. All HRs were adjusted for the following nine potential confounding factors: 1) age (continuous variable), 2) sex (male or female), 3) comorbidity (categorised into 0, 1 or ≥2 according to the Charlson Index Scoring System),[19] 4) neoadjuvant therapy (yes or no), 5) tumour stage (0-I, II, III or IV), 6) placement of a feeding jejunostomy (yes or no), 7) surgical approach (oesophagectomy, extended total gastrectomy or oesophagogastrectomy), 8) histological type of tumour (adenocarcinoma or squamous-cell carcinoma), and 9) education (≤9, 10–12, or >12 years of formal education). Additionally, the HRs evaluating post-operative weight change were further adjusted for pre-operative weight change, the HRs of BMI at operation were further adjusted for pre-operative weight change, and the HRs of BMI at 6 months were further adjusted for pre to post-operative weight change. Pre-operative, post-operative and pre to post-operative (total) weight changes were categorised into weight gain or stable weight [+/−1%]; 1.1–10% weight