

Nowadays, there is still no consensus about the benefits of adding neck lymphadenectomy to the traditional two-fields esophagectomy. An extended lymphadenectomy could potentially increase operation time and the risks for postoperative complications. However, extended lymphadenectomy allows resection of cervical nodes at risk for metastases, potentially increasing long-term survival rates. This study aims to estimate whether cervical prophylactic lymphadenectomy for esophageal cancer influences short- and long-term outcomes through a systematic review of literature and meta-analysis.

Methods: A systematic review was conducted in PubMed, Embase, Cochrane Library Central, and Lilacs (BVS). The inclusion criteria were: (1) studies that compare two-field vs. three-field esophagectomy; (2) adults (>18 years); (3) articles that analyze short- or long-term outcomes; and (4) clinical trials or cohort studies. The results were summarized by forest plots, with effect size (ES) or risk difference (RD) and 95% CI.

Results: Twenty-five articles were selected, comprising 8,954 patients. Three-field lymphadenectomy was associated to higher operation time (ES: -1.51; 95%CI -1.84, -1.18) and higher blood loss (ES: -0.24; 95%CI: -0.37, -0.11). Also, neck lymphadenectomy inputs additional risk for pulmonary complications (RD: 0.03; 95%CI: 0.01, 0.05). No difference was noted for morbidity (RD: 0.01; 95%CI: -0.01, 0.03); leak (-0.02; 95%CI: -0.07, 0.03); postoperative mortality (RD: 0.00; 95%CI: -0.00, 0.01), and hospital stay (ES: -0.05; 95%CI -0.20, 0.10). Three-field lymphadenectomy allowed higher number of retrieved lymph nodes (MD: -1.51; 95%CI -1.84, -1.18), but did not increase the overall survival (HR: 1.11; 95%CI: 0.96, 1.26).

Conclusion: Prophylactic neck lymphadenectomy for esophageal cancer should be performed with caution once it is associated with poorer short-term outcomes compared to traditional two-field lymphadenectomy and does not improve long-term survival. Future esophageal cancer studies should determine the subgroup of patients who could benefit from prophylactic neck lymphadenectomy in long-term outcomes.

727 EXOCRINE PANCREATIC INSUFFICIENCY AFTER ESOPHAGECTOMY: A SYSTEMATIC REVIEW OF LITERATURE

Lotte Blomk,^{1,2} N.J. Wierdsma,² E.P. Jansma,³ G. Kazemier,¹ D.L. Peet, van der¹ J. Straatman,¹

1. Amsterdam UMC, Cancer Center Amsterdam, Department of Surgery, Vrije Universiteit Amsterdam, Amsterdam, The Netherlands 2. Amsterdam UMC, Department of Nutrition and Dietetics, Vrije Universiteit Amsterdam, Amsterdam, The Netherlands 3. Medical Library, Vrije Universiteit Amsterdam, Amsterdam, The Netherlands

Complaints of maldigestion, malabsorption, and unintended weight loss after esophagectomy are often attributed to an impaired exocrine pancreatic function. This review systematically summarizes all literature reporting on the presence of exocrine pancreatic insufficiency (EPI) after esophagectomy and the effect of treatment with pancreatic enzymes on gastrointestinal complaints, body weight, and quality of life.

Methods: Databases of PubMed, Embase, and Wiley/Cochrane Library were searched systematically until July 2020. Studies reporting on EPI and pancreatic enzyme replacement therapy after esophagectomy were included.

Results: Four studies, including 158 patients, were selected. Exocrine pancreatic function was investigated in three studies, measured by fecal elastase-1 and 72-hour fecal fat excretion. Fecal elastase-1 levels <200 µg/g were reported in 16% of patients at 4 months, 18% at 6 months, and 31% at 18-24 months postoperatively. A decreased fecal fat absorption was noticed in 57% 1 month postoperatively. Treatment with pancreatic enzymes was reported in two studies. In patients with fecal elastase-1 levels <200 µg/g, 90% of patients reported improvement in symptoms and 70% reported improvement in weight. In patients with complaints of steatorrhea, 87% noticed settlement of symptoms.

Conclusion: Based on current literature, complaints of maldigestion, malabsorption, and unintended weight loss after esophagectomy are common and can be related to an impaired exocrine pancreatic function. High-quality studies evaluating the presence of EPI and the effect of treatment with pancreatic enzymes after esophagectomy are needed to verify this conclusion.

729 RELATION OF POSTOPERATIVE MORBIDITY WITH QUALITY OF LIFE FOLLOWING ESOPHAGEAL SURGERY FOR CANCER: A EUROPEAN MULTICENTER STUDY

Nannet Schuring,¹ Sheraz R. Markar,² Egle Jezerskyte,¹ Mirjam A.G. Sprangers,¹ Asif Johar,³ Mark I. Berge Henegouwen, van¹ Suzanne S. Gisbertz,¹

1. Amsterdam UMC, Amsterdam, the Netherlands 2. Imperial College, London, United Kingdom 3. Karolinska Institutet, Stockholm, Sweden 4. LASER study group

Despite improvements in perioperative esophageal cancer care, severe post-operative complications occur in 17.2% of the patients. Postoperative complications are associated with reduced health-related quality of life (HR-QoL), and severe complications may have a profound negative effect on the HR-QoL. The aim of this study was to investigate the relation between postoperative morbidity and reported HR-QoL in patients following esophagectomy for cancer.

Methods: Disease-free patients at least one year following esophagectomy for cancer in one of the participating LASER study centers between 2010 and 2016 were included. Patients completed the LASER, EORTC-QLQ-C30 and QLQ-OG25 questionnaires at least one year following surgery. The primary outcome was the relation between reported HR-QoL and occurrence of postoperative complications and to compare the HR-QoL in the study population with the reference values of the general population. Subgroup analysis was performed in patients with 'no' or 'minor' (Clavien-Dindo grade I-IIIa) and 'severe' (Clavien-Dindo grade ≥ IIIb) complications, using univariable and multivariable logistic regression analysis.

Results: Among 645 included patients, 283 patients with 'no', 207 patients with 'minor' and 155 patients with 'severe' postoperative complications were included. The mean age of the patients was 64 years (SD 9), with a mean time since surgery of 4.4 years (SD 1.7). Neither significant or clinically relevant differences were found in the HR-QoL scores between patients with and without complications, nor were differences observed in subgroup analysis for severity of postoperative complications. Compared to the general population, patients reported worse HR-QoL in all domains except 'Global Health' and 'Emotional Functioning', and more symptomatology in all symptom domains except 'Pain'.

Conclusion: HR-QoL between patients at a median of 4.4 years after esophagectomy for cancer did not differ. Differences were neither significant nor clinically relevant and furthermore, no differences were observed in subgroup analysis for severity of postoperative complications according to Clavien-Dindo.

731 RISK OF ESOPHAGEAL AND GASTRIC ADENOCARCINOMA IN MEN RECEIVING ANDROGEN DEPRIVATION THERAPY FOR PROSTATE CANCER

Richard Shore,¹ Jingru Yu,¹ Weimin Ye,¹ Jesper Lagergren,¹ Martin Rutegård,² Olof Akre,¹ Pär Stattin,³ Mats Lindblad,¹

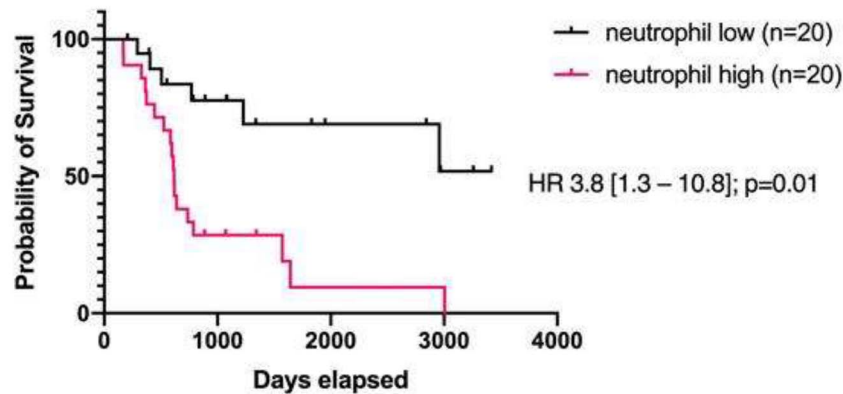
1. Karolinska Institutet, Stockholm, Sweden 2. Umeå University, Umeå, Sweden 3. Uppsala University, Uppsala, Sweden

There is an unexplained male predominance in the incidence of esophageal (EAC) and non-cardia gastric adenocarcinoma (GAC) which cannot be explained by known risk factors. Differences in the exposures to sex hormones may play a part in the observed sex difference. This study aimed to test the hypothesis that androgens increase the risk of EAC, cardia GAC, and non-cardia GAC. We analysed a matched cohort based on a national Swedish database of prostate cancer patients.

Methods: Prostate cancer patients receiving androgen deprivation therapy (ADT) were the exposed group. Prostate cancer-free men from the general population were randomly selected and matched to the index case by birth year and county of residence, forming the unexposed control group. The participants were followed until a diagnosis of esophageal or gastric cancer, death, emigration, or end of the study period. The risk of esophageal adenocarcinoma, cardia gastric adenocarcinoma, non-cardia gastric adenocarcinoma, and esophageal squamous-cell carcinoma among ADT-exposed compared to unexposed was calculated by multivariable Cox proportional hazard regression. The hazard ratios and 95% confidence intervals were adjusted for confounders.

Results: There was a risk reduction of non-cardia gastric adenocarcinoma among ADT-users compared to non-users (HR 0.49 [95% CI 0.24-0.98]).

Neutrophil infiltration and DSS in patients with residual disease



No such decreased risk was found for esophageal adenocarcinoma (HR 1.17 [95% CI 0.60–2.32]), cardia gastric adenocarcinoma (HR 0.99 [95% CI 0.40–2.46]), or esophageal squamous cell carcinoma (HR 0.99 [95% CI 0.31–3.13]).

Conclusion: This study indicates that androgen deprivation therapy decreases the risk of non-cardia gastric adenocarcinoma, while no decreased risk was found for esophageal adenocarcinoma, cardia gastric adenocarcinoma, or esophageal squamous-cell carcinoma.

732 TUMOR INFILTRATING NEUTROPHILS ARE A POOR PROGNOSTIC MARKER FOR ESOPHAGEAL CANCER PATIENTS RECEIVING NEOADJUVANT CHEMORADIO THERAPY

Carlos Cabalag,^{1,2} Owen Prall,¹ John Ciciulla,³ Laurence Galea,³ Niko Thio,¹ Lynn Chong,⁴ Michael W Hii,⁴ Paul J Neeson,¹ Gisela Mir Arnau,¹ Wayne A Phillips,^{1,2,4} Nicholas J Clemons,^{1,2} Cuong P Duong,^{1,2}

1. Peter MacCallum Cancer Centre, Melbourne, Australia 2. Sir Peter MacCallum Department of Oncology, Melbourne, Australia 3. Melbourne Pathology, Melbourne, Australia 4. University of Melbourne Department of Surgery St. Vincent's Hospital, Melbourne, Australia

Significant advances have been made in our understanding of the tumor immune microenvironment (TIM) and tumor infiltrating lymphocytes (TILs). Nevertheless, there is little understanding of the changes in the TIM in response to neoadjuvant chemoradiotherapy (CRT). Thus, our aim was to investigate the changes in the TIM with neoadjuvant CRT in EC by assessing the immune cell infiltrate, the expression of immune related genes, and their association with treatment response and prognosis.

Methods: To decipher the effects of neoadjuvant CRT on the TIM, we obtained 58 paired pre-treatment and post neoadjuvant CRT treated EC specimens. TILs and tumor infiltrating neutrophils (TIN) were quantified in pre-treatment biopsies and surgical resection specimens following neoadjuvant CRT. To evaluate the immune transcriptomics, RNA was extracted from these specimens and gene expression was assessed using the Nanostring Platform based on the PanCancer Immune Profiling Panel. Immunohistochemistry (IHC) was performed to validate findings from the immune transcriptomics.

Results: TIL counts were not prognostic for disease specific survival (DSS). We observed higher expression of immune-suppressive inflammatory chemokines (TGF β -1 and IL-16) in post-neoadjuvant treated samples compared to pre-treatment biopsies. In samples collected after neoadjuvant CRT, low expression of genes related to anti-tumor T cell cytotoxic activity was significantly associated with disease recurrence. In patients with residual disease, multivariate analysis revealed a high neutrophil count, but not TIL count, was significantly associated with inferior DSS (HR 3.8 [1.3– 10.8]; p=0.01).

Conclusion: In EC, the tumor microenvironment after neoadjuvant CRT remains largely immune-suppressive. We discovered that the presence of TINs in patients with residual disease post neoadjuvant CRT is an independent adverse prognostic factor. Collectively, our results suggest that an inflammatory pro-tumoral microenvironment associated with TINs may contribute to treatment resistance and progressive disease in EC.

734 PL11.06 PROGNOSTIC FACTORS FOR MORTALITY IN PATIENTS WITH ANASTOMOTIC LEAKAGE AFTER ESOPHAGECTOMY FOR CANCER (TENTACLE—ESOPHAGUS STUDY)

Sander Ubels,¹ Moniek Verstegen,¹ Stefan Bouwense,² Gerjon Hannink,³ Bastiaan Klarenbeek,¹ Peter Siersema,⁴ Frans Workum, van^{1,5} Camiel Rosman,¹ on behalf of the TENTACLE - Esophagus Collaborative group

1. Department of Surgery, Radboudumc, Nijmegen, Netherlands 2. Department of Surgery, Maastricht UMC+, Maastricht, Netherlands 3. Department of Operating Rooms, Radboudumc, Nijmegen, Netherlands 4. Department of Gastroenterology and Hepatology, Radboudumc, Nijmegen, Netherlands 5. Department of Surgery, Canisius-Wilhelmina Hospital, Nijmegen, Netherlands

Anastomotic leakage (AL) is a common and potentially life-threatening complication after esophagectomy. In patients with AL it is largely unknown which patient parameters and leakage characteristics are associated with leak severity and mortality. We aimed to identify prognostic factors for mortality in patients with anastomotic leakage after esophagectomy.

Methods: The TENTACLE—Esophagus study is an international retrospective cohort study, in which 1451 patients with AL after esophagectomy between 2011 and 2019 were included in 71 centers from 20 countries. Potential prognostic factors were selected from literature and a hypothetical association with mortality. Confounders of (individual) prognostic factors were identified using a directed acyclic graph approach to minimize bias. Primary outcome was 90-day mortality. Logistic regression analysis was performed to estimate crude and adjusted odds ratios (AOR) and 95% confidence intervals (95%CI). The study protocol is accessible at www.tentaclestudy.com.

Results: Overall 90-day mortality rate was 11.6%. Leakage characteristics with the largest prognostic effect on mortality were gastric conduit ischemia/necrosis (AOR 2.23, 95%CI 1.43-3.49), defect circumference \geq 25% (AOR 2.10, 95%CI 1.32-3.36) and intrathoracic fluid collections (drained AOR 1.98, 95%CI 1.05-3.75; undrained AOR 2.43, 95%CI 1.57-3.75). Patient parameters with the largest prognostic effect were ASA-score \geq 3 (AOR 4.18, 95%CI 1.67-10.51), ECOG-score \geq 2 (AOR 2.83, 95%CI 1.56-5.14) and respiratory failure (AOR 3.89, 95%CI 2.67-5.66), hemodynamic failure (AOR 3.09, 95%CI 1.96-4.88) or renal failure (AOR 4.08, 95%CI 2.20-7.59) at time of AL diagnosis.

Conclusion: Defect circumference, intrathoracic fluid collections, gastric conduit condition and several patient parameters were identified as prognostic factors for mortality in patients with AL. Adjusting for these prognostic factors may reduce confounding bias in future studies assessing efficacy of AL treatments. The identified prognostic factors contribute to the understanding of the severity of anastomotic leakage after esophagectomy and may be used to recognize the severity of an anastomotic leak in individual patients.

736 PL11.04 HEALTH-RELATED QUALITY OF LIFE OF PATIENTS WITH ESOPHAGEAL CANCER FOLLOWING ESOPHAGECTOMY TREATED WITH NEOADJUVANT CHEMORADIO THERAPY OR CHEMOTHERAPY: EUROPEAN MULTICENTER STUDY

Nannet Schuring,¹ Sheraz Markar,² Eliza R.C. Hagens,¹ Egle Jezerskyte,¹ Mirjam A.G. Sprangers,¹ Asif Johar,³ Suzanne S. Gisbertz,¹ Mark I. Berge Henegouwen, van¹