Nutritional jejunostomy in esophagectomy for cancer, a national register-based cohort study of associations with postoperative outcomes and survival

Anders Holmén¹,² · Masaru Hayami¹,³ · Eva Szabo⁴,⁵ · Ioannis Rouvelas¹,³ · Thorhallur Agustsson²,⁶ · Fredrik Klevebro¹,³

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Abstract

Purpose Insertion of a nutritional jejunostomy in conjunction with esophagectomy is performed with the intention to decrease the risk for postoperative malnutrition and improve recovery without adding significant catheter-related complications. However, previous research has shown no clear benefit and there is currently no consensus of practice.

Methods All patients treated with esophagectomy due to cancer during the period 2006–2017 reported in the Swedish National Register for Esophageal and Gastric Cancer were included in this register-based cohort study from a national database. Patients were stratified into two groups: esophagectomy alone and esophagectomy with jejunostomy.

Results A total of 847 patients (45.27%) had no jejunostomy inserted while 1024 patients (54.73%) were treated with jejunostomy. The groups were comparable, but some differences were seen in histological tumor type and tumor stage between the groups. No significant differences in length of hospital stay, postoperative surgical complications, Clavien-Dindo score, or 90-day mortality rate were seen. There was no evidence of increased risk for significant jejunostomy-related complications. Patients in the jejunostomy group with anastomotic leaks had a statistically significant lower risk for severe morbidity defined as Clavien-Dindo score ≥ IIIb (adjusted odds ratio 0.19, 95% CI: 0.04–0.94, P = 0.041) compared to patients with anastomotic leaks and no jejunostomy.

Conclusion A nutritional jejunostomy is a safe method for early postoperative enteral nutrition which might decrease the risk for severe outcomes in patients with anastomotic leaks. Nutritional jejunostomy should be considered for patients undergoing curative intended surgery for esophageal and gastro-esophageal junction cancer.

Keywords Esophageal cancer · Esophagectomy · Postoperative complications · Anastomotic leak · Feeding jejunostomy

Introduction

Postoperative complications after esophagectomy are common [1] and associated with increased mortality [2–4] and long-term decreased health-related quality of life (HRQOL) [5, 6].

Esophagogastric anastomotic leak is the major complication after esophagectomy, with a reported incidence of 4–35% [1, 7, 8]. Patients who suffer an anastomotic leak have an almost tenfold increase in the 30-day mortality rate from 2–3% to 17–35% [2]. Anastomotic leaks are associated with a nutritional deficit, which can make recovery difficult.

Nutrition is fundamental for the successful treatment of esophageal cancer where malnutrition, weight loss, and cancer cachexia are particularly prevalent [9]. Early postoperative enteral nutrition has proven to be clearly beneficial and is a key component of the ERAS protocol [10]. Enteral nutrition is
associated with improved levels of gut oxygenation, lower
costs, and reduced postoperative length of stay compared with
total parenteral nutrition [11–13].

Insertion of a nutritional jejunostomy is made with the in-
tent to secure a nutritional route, should postoperative oral
feeding be contraindicated or insufficient. The jejunostomy
can be used to give full enteral nutrition after surgery or for
nutritional support in combination with early oral feeding de-
pending on the applied clinical pathway. There is a risk for
catheter-related complications, most of which are minor, such
as local skin contamination, dislocation, catheter site infect-
tion, and occlusion [14]. Severe complications such as small
bowel necrosis and intestinal torsion are rare but potentially
life-threatening [15–17].

The aim of this study was to determine if the insertion of a
nutritional jejunostomy in conjunction with esophagectomy
for cancer was associated with decreased postoperative mor-
bidity. The secondary outcome was to evaluate if the oppor-
tunity to give enteral nutrition with the use of a jejunostomy
was associated with improved outcomes for patients with the
postoperative anastomotic leak.

**Methods**

**Study design**

A nationwide, retrospective, population-based cohort study
from a prospectively collected national database including all
patients undergoing esophageal cancer surgery in Sweden be-
tween 2006 and 2017 was performed. Data was collected from
the Swedish National Register for Esophageal and Gastric
Cancer, in which all patients with esophageal or gastro-
esophageal cancer in Sweden are included. The register has a
national coverage of 95.5% and an overall accuracy of 91%
[18]. The clinical data include patient and tumor characteristics,
treatment details regarding oncological and surgical manage-
ment (including the insertion of a jejunostomy or not), and study
outcomes.

**Exposure**

Study exposure was the insertion of nutritional jejunostomy in
conjunction with esophagectomy for cancer of the esophagus
or the gastro-esophageal junction.

**Outcomes**

All clinical data were collected from the register. Enrolled
patients were cross-matched with the National Cause of
Death Register via the individual unique personal identifica-
tion number assigned to all Swedish residents [19]. Outcomes
included overall postoperative complications stratified by
surgical or non-surgical complications, with surgical compli-
cations defined as follows: Postoperative leakage was con-
ﬁrmed with CT scan, with an oral water-soluble contrast me-
dium, or veriﬁed with endoscopy. Conduit necrosis was de-
ﬁned as conﬁrmed ischemia of the conduit with perforation or
ulcer. Bleeding was deﬁned as blood loss of more than 2 L or
need of surgical re-intervention. Chylothorax was deﬁned as a
leak that required drainage for more than 7 days or a need for
surgical re-intervention. Recurrent nerve paralysis was con-
ﬁrmed by an otorhinolaryngologist. Abdominal or thoracic
abscesses were reported when the size of the abscess exceeded
3 × 3 cm and was veriﬁed radiologically or surgically.

Included among the non-surgical complications were car-
diac arrhythmias requiring medical treatment, myocardial in-
farction, and cerebral embolism. Pulmonary embolism was
defined as radiographically conﬁrmed embolus requiring treat-
ment. The deﬁnition of respiratory failure was when pa-
tients required invasive or non-invasive ventilation. Pneumonia
was deﬁned as x-ray-conﬁrmed inﬁltration combined with fever,
cough, and/or dyspnea and infections non-
related to the operation ﬁeld. Septicemia was deﬁned as a
body temperature above 38.3 °C (101 °F) or below 36 °C
(96.8 °F) with a positive blood culture. Length of hospital stay
in days and overall all-cause mortality were calculated based
on data from the National Cause of Death Register.

**Statistical methods**

Multivariable logistic regression modeling, chi-square test, and
Fisher’s exact test were used for binomial outcomes. The mul-
tivariable logistic regression model and the Cox proportional
hazard model were pre-speciﬁed and included tumor histology,
clinical tumor stage, tumor location, and ASA score. Complete
case analysis was performed in the multivariable-adjusted mod-
el. The categorizations of the variables are displayed in Table 1.
The Cox proportional hazard model was used for the survival
analyses. The proportional hazard assumptions were tested in
all models using the Grambsch and Therneau test based on
Schoenfeld residuals, which did not show any violations. For
each outcome, we report the odds ratio (OR) and 95% conﬁdence
interval (CI). The significance level was set at 0.05. Analyses were performed using STATA® version 13 software
(StataCorp LP, College Station, Texas, USA).

**Results**

**Patient demographics and baseline characteristics**

Out of the 1871 patients who underwent surgery for esopha-
geal or gastro-esophageal junction cancer, 847 (45.3%) were
treated with no jejunostomy and 1024 (54.7%) with nutrition-
al jejunostomy. The groups were similar with regard to age,
gender, body weight, performance status, ASA score, and dysphagia score (Table 1).

Tumor characteristics and treatment details

Jejunostomies were less frequently inserted in cT1 tumors (12.5% vs. 7.0%) and slightly more often in T2 and T3 tumors (25.4% vs. 29.1%, 46.5% vs. 48.1%, $P=0.002$). No significant differences were found concerning clinical N-stage, tumor location, preoperative treatment, or surgical approach. Jejunostomy was more often used with a transthoracic and transhiatal approach compared to gastrectomy ($P=0.001$, Table 2). Histological tumor type was different between the groups ($P=0.005$), with a higher tumor burden in the jejunostomy group. There was no significant difference in neoadjuvant treatment. Jejunostomies were inserted with open technique in 852 (83.2%) patients and laparoscopic technique in 172 patients (16.8%, Table 3). The register had some missing data concerning clinical T-stage (219 patients, 11.7%), N-stage (92 patients, 4.9%), tumor location (220 patients, 11.8%), surgical technique (98 patients, 5.2%), and histological tumor type (24 patients, 1.3%) (Table 2).

Short-term clinical outcomes and survival

Postoperative complications were reported in 330 (39.0%) patients with no jejunostomy and in 454 (44.4%) patients with jejunostomy ($P=0.019$). No significant differences in severity of complications according to the Clavien-Dindo scoring system were observed. Missing data concerning Clavien-Dindo score was reported in 211/784 (26.9%) of the patients with complication. The median length of hospital stay was similar. No significant differences were seen concerning the incidence of anastomotic leak, gastric conduit necrosis, re-operations, or occurrences of thoracic abscesses. Recurrent laryngeal nerve paralysis was more frequently reported in patients with jejunostomy (2.5% vs 4.3%, $P=0.033$) as were non-surgical complications (22.2% vs 29.8%, $P<0.001$) such as pneumonia (7.2% and 11.8%, $P=0.001$). The postoperative 90-day mortality was 6.9% in patients without jejunostomy and 5.1% in the jejunostomy group ($P=0.105$, Table 3).

No significant differences were observed comparing open to laparoscopic jejunostomy concerning postoperative complications, surgical complications, re-operations, or Clavien-Dindo score $\geq$ IIIb (Table 3).

Multivariable adjusted analyses showed a statistically significant increase in risk for postoperative non-surgical

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**Table 1 Baseline characteristics of patients undergoing esophagectomy for esophageal or gastro-esophageal junction cancer, stratified by nutritional jejunostomy**

|                          | No jejunostomy | Jejunostomy | $P$ value |
|--------------------------|----------------|-------------|-----------|
| Total                    | 847 (45.3)     | 1024 (54.7) | 0.999     |
| Age, median (range)      | 66 (20–93)     | 66 (29–88)  | 0.999     |
| Gender                   |                |             | 0.763     |
| Male                     | 671 (79.2)     | 817 (79.8)  |           |
| Female                   | 176 (20.8)     | 207 (20.2)  |           |
| Mean body weight in kg (range) |80.8 (47–141) | 81.3 (51–137)| 0.999     |
| Performance status       |                |             | 0.104     |
| 0                        | 452 (57.1)     | 598 (61.9)  |           |
| 1                        | 291 (36.8)     | 322 (33.3)  |           |
| 2                        | 48 (6.1)       | 46 (4.8)    |           |
| Unknown                  | 56             | 58          |           |
| ASA score                |                |             | 0.458     |
| I                        | 292 (35.9)     | 347 (35.6)  |           |
| II                       | 397 (48.8)     | 475 (48.7)  |           |
| III                      | 116 (14.3)     | 150 (15.4)  |           |
| IV                       | 8 (1.0)        | 4 (0.4)     |           |
| Unknown                  | 34             | 48          |           |
| Baseline dysphagia score |                |             | 0.765     |
| No dysphagia             | 76 (32.8)      | 64 (30.9)   |           |
| Dysphagia to solid food  | 108 (46.6)     | 103 (49.8)  |           |
| Dysphagia to semi-solid food |33 (14.2)     | 30 (14.5)   |           |
| Dysphagia to liquids     | 14 (6.0)       | 8 (3.9)     |           |
| Total dysphagia          | 1 (0.4)        | 2 (1.0)     |           |
| Unknown                  | 615            | 817         |           |
complications, pneumonia, septicemia, and recurrent nerve paralysis in the jejunostomy group (Table 4). There was no significant difference in long-term survival between the groups (Fig. 1).

**Clavien-Dindo score ≥ IIIb and 90-day mortality in patients with complications**

Any postoperative complication within 90 days was evaluated with adjusted logistic regression analysis to assess the impact on risk for Clavien-Dindo score ≥ IIIb, as well as 90-day postoperative mortality in patients with complications comparing the no jejunostomy group to the jejunostomy group. In patients with postoperative anastomotic leakage, the odds ratio for Clavien-Dindo score ≥ IIIb was 0.19 (95% CI: 0.04–0.94) compared to patients without jejunostomy. There were no significant differences in the odds ratios for Clavien-Dindo score ≥ IIIb concerning other postoperative complications or 90-day mortality. In patients with anastomotic leakage, the odds ratio for 90-day mortality in the jejunostomy group was 0.53 (95% CI: 0.24–
1.19) compared to patients with no jejunostomy. For patients with postoperative chylothorax, the corresponding odds ratio was 0.21 (95% CI: 0.03–1.33, Table 5).

**Discussion**

The results of this population-based cohort study demonstrate that the insertion of a feeding jejunostomy in conjunction with esophagectomy was not associated with an overall increased risk for postoperative surgical complications. However, nonsurgical complications, such as pneumonia and septicemia, were more common in the jejunostomy group which might be explained by confounding factors such as surgical technique and increased use of jejunostomy for patients with more locally advanced tumors. The study shows that jejunostomy in patients with the anastomotic leak was associated with a significantly lower risk for Clavien-Dindo score ≥IIIb, which suggests that jejunostomy in conjunction with esophagectomy might increase the chance to recover from an anastomotic leak without re-operation and intensive care. A jejunostomy provides a secure route for enteral nutrition in the event of an anastomotic leak which might explain the observed improved outcome in the jejunostomy group.

The observed higher incidence of pneumonia in the jejunostomy group is, to our knowledge, not previously
demonstrated and is contradictory to results shown elsewhere [20, 21]. Although it might reflect the association between jejunostomy and small bowel obstruction, as has been suggested by Koterazawa et al. [22], this was not seen in our study. Among surgical complications, the only statistically significant finding was an increased frequency of recurrent laryngeal nerve paralysis in the jejunostomy group. While this is unlikely to be related to the insertion of a jejunostomy, it is worth to notice. The increased incidence of pneumonia observed in the jejunostomy group might be explained by the higher incidence of recurrent laryngeal nerve paralysis in the jejunostomy group in terms of higher risk for aspiration. The results show a selection bias towards jejunostomy in more frail patients with a higher incidence of squamous cell carcinoma and a more advanced tumor stage. These patients require a more extensive lymph node dissection in the upper mediastinum which might explain the higher incidence of recurrent nerve palsy. The increased risk for non-surgical complications may also be explained by the increased use of jejunostomies in patients with more advanced tumor stages and in patients with the preoperative nutritional deficit, something that should be further assessed in future studies. Factors concerning baseline characteristics and type of surgery were included in the multivariable-adjusted model but there is a risk for residual confounding.

Data concerning preoperative nutritional status such as BMI and weight loss is not included in the register. High-quality data concerning weight loss is hard to evaluate since no measurements are recorded before the diagnosis. Secondary measurements concerning nutritional status such

|                | No jejunostomy | Jejunostomy | P value |
|----------------|----------------|-------------|---------|
| Any complication | 1.0 (reference) | 1.28 (1.06–1.55) | 0.011  |
| Surgical complication | 1.0 (reference) | 1.07 (0.87–1.33) | 0.506  |
| Anastomotic leak | 1.0 (reference) | 1.21 (0.89–1.65) | 0.226  |
| Chylothorax | 1.0 (reference) | 0.83 (0.48–1.44) | 0.507  |
| Recurrent laryngeal nerve paralysis | 1.0 (reference) | 1.94 (1.11–3.38) | 0.020  |
| Non-surgical complication | 1.0 (reference) | 1.53 (1.23–1.90) | < 0.001 |
| Cardiovascular complication | 1.0 (reference) | 1.40 (0.92–2.14) | 0.117  |
| Pulmonary embolism | 1.0 (reference) | 1.72 (0.92–3.21) | 0.089  |
| Pneumonia | 1.0 (reference) | 1.79 (1.29–2.48) | 0.001  |
| Septicemia | 1.0 (reference) | 1.54 (1.01–2.34) | 0.043  |
| Clavien-Dindo ≥ IIIb | 1.0 (reference) | 1.16 (0.81–1.65) | 0.423  |

†Adjusted for histological tumor type, clinical tumor stage, and American Society of Anesthesiologists Score

Fig. 1 Kaplan-Meier survival curve stratified by esophagectomy with or without nutritional jejunostomy for patients treated for esophageal or gastro-esophageal junction cancer (P = 0.417)
as mean body weight and baseline dysphagia score are however registered and were similar between the two groups. From the accessible data, preoperative nutritional status seems to have a minor impact on the decision to provide patients with a jejunostomy; local protocols are likely to have a more important role. It is however worth considering the risk for selection bias in the study.

Perioperative management including postoperative nutritional details or information about nasogastric tubes or early feeding is unfortunately not included in the register data. This study has analyzed the effects of the insertion of a jejunostomy at the time of the esophagectomy. A future study with more detailed data about oral, enteral, and parenteral nutrition after surgery is planned within our group.

Jejunostomy treatment details such as duration of catheter placement, degree of jejunostomy utilization, and minor jejunostomy-related complications would have been valuable to analyze, but this level of granularity of data is unfortunately not recorded in the register. However, no difference in surgical complications, Clavien-Dindo score, or re-operation was observed between the groups, which indicates that jejunostomy was not associated with increased risk for significant postoperative surgical complications.

Clavien-Dindo score was included in the register from 2012, and consequently, 211/784 (26.9%) of the patients with complication had missing data concerning Clavien-Dindo score. This is a weakness of the study; however, it is likely that this is proportionally distributed randomly between the groups. Missing data concerning tumor stage, surgical technique, and histological tumor type was taken into consideration as a complete case analysis was performed in the multivariable-adjusted model.

Strengths of the study include the population-based design, a relatively large cohort with a near-complete national coverage of all patients who underwent surgical resection for esophageal cancer in Sweden during the study period, small numbers of missing data, and the complete follow-up concerning survival made possible by the use of the National Cause of Death Register [19].

Previous research has shown that nutritional jejunostomies as part of curative treatment of esophageal cancer are safe, but controversy exists on the practice of routinely doing so, as evidence of its benefits in general is lacking [20, 23]. The nutritional deficit, weight loss, and sarcopenia are major issues that require intervention for patients undergoing esophageal cancer treatment. Jejunostomy insertion before the start of neoadjuvant treatment might provide an even more efficient nutritional treatment in selected patients [21, 24]. It is, however, challenging to design high-quality studies about nutritional treatments. Future studies need to focus on identifying

| Table 5 Risk for Clavien-Dindo score ≥ IIIb and 90-day mortality comparing patients with jejunostomy vs. no jejunostomy in patients with postoperative complications after esophagectomy for cancer |
|-------------------------------------------------------------|
|                                                                 |
| Clavien-Dindo score ≥ IIIb                                  |
| Any complication                                             |
| 1.0 (reference)                                              |
| 1.09 (0.72–1.65)                                             |
| 0.689                                                       |
| Surgical complication                                        |
| 1.0 (reference)                                              |
| 1.07 (0.62–1.85)                                             |
| 0.815                                                       |
| Anastomotic leak                                             |
| 1.0 (reference)                                              |
| 0.19 (0.04–0.94)                                             |
| 0.041                                                       |
| Chylothorax                                                  |
| 1.0 (reference)                                              |
| 0.67 (0.10–4.51)                                             |
| 0.682                                                       |
| Recurrent laryngeal nerve paralysis                           |
| 1.0 (reference)                                              |
| 1.48 (0.29–7.51)                                             |
| 0.633                                                       |
| Non-surgical complication                                    |
| 1.0 (reference)                                              |
| 1.56 (0.92–2.63)                                             |
| 0.099                                                       |
| Cardiovascular complication                                  |
| 1.0 (reference)                                              |
| 2.24 (0.66–7.57)                                             |
| 0.196                                                       |
| Pulmonary embolism                                           |
| 1.0 (reference)                                              |
| 0.80 (0.15–4.12)                                             |
| 0.788                                                       |
| Pneumonia                                                    |
| 1.0 (reference)                                              |
| 1.64 (0.71–3.79)                                             |
| 0.248                                                       |
| Septicemia                                                   |
| 1.0 (reference)                                              |
| 0.82 (0.16–4.30)                                             |
| 0.817                                                       |

| 90-day mortality                                            |
|-------------------------------------------------------------|
| Any complication                                             |
| 1.0 (reference)                                              |
| 0.85 (0.53–1.36)                                             |
| 0.498                                                       |
| Surgical complication                                        |
| 1.0 (reference)                                              |
| 0.71 (0.40–1.25)                                             |
| 0.238                                                       |
| Anastomotic leak                                             |
| 1.0 (reference)                                              |
| 0.53 (0.24–1.19)                                             |
| 0.125                                                       |
| Chylothorax                                                  |
| 1.0 (reference)                                              |
| 0.21 (0.03–1.33)                                             |
| 0.098                                                       |
| Recurrent nerve paralysis                                    |
| 1.0 (reference)                                              |
| 0.59 (0.03–13.49)                                            |
| 0.740                                                       |
| Non-surgical complication                                    |
| 1.0 (reference)                                              |
| 0.76 (0.44–1.29)                                             |
| 0.309                                                       |
| Cardiovascular complication                                  |
| 1.0 (reference)                                              |
| 0.95 (0.31–2.88)                                             |
| 0.922                                                       |
| Pulmonary embolism                                           |
| 1.0 (reference)                                              |
| 0.86 (0.13–5.87)                                             |
| 0.877                                                       |
| Pneumonia                                                    |
| 1.0 (reference)                                              |
| 0.68 (0.26–1.78)                                             |
| 0.431                                                       |
| Septicemia                                                   |
| 1.0 (reference)                                              |
| 0.74 (0.26–2.09)                                             |
| 0.572                                                       |

†Adjusted for histological tumor type, clinical tumor stage, and American Society of Anesthesiologists Score
patients who may benefit most from a nutritional jejunostomy, timing of placement, how and when it should be used, and also monitor changes in body composition prior to and during multimodality treatment, preferably in a randomized design.

In conclusion, this study indicates that a nutritional jejunostomy might decrease the risk for severe outcomes in patients with postoperative anastomotic leak after esophagectomy. However, our data suggests no clear benefit to apply standardized nutritional jejunostomy to all esophagectomy patients. Future research needs to investigate the optimal use of nutritional jejunostomy in esophageal cancer treatment.

Authors’ contributions Study conception and design: Holmén, Hayami, Szabo, Rouvelas, Agustsson, Klevebro; acquisition of data: Holmén, Hayami, Rouvelas, Klevebro; analysis and interpretation of data: Holmén, Hayami, Agustsson, Klevebro; drafting of manuscript: Holmén, Klevebro, Agustsson, Rouvelas; critical revision of manuscript: Holmén, Hayami, Szabo, Rouvelas, Agustsson, Klevebro.

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Compliance with ethical standards

Conflict of interest The authors have declared no conflicts of interest.

Ethical approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. Approval for the study was granted by the Regional Ethical Review Board in Stockholm, Sweden (Dnr 2013/596-31/3).

Informed consent For the present study, no informed consent was required. This was approved by the Regional Ethical Review Board in Stockholm, Sweden.

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