

Operative outcomes and long-term survival of patients undergoing colon interposition after esophagectomy for cancer

Tomohiro Akutsu¹ | Takeo Fujita¹  | Daisuke Kajiyama¹ | Asako Ozaki¹ | Kazuma Sato¹ | Hisashi Fujiwara¹ | Takashi Kojima² | Hiroyuki Daiko³

¹Division of Esophageal Surgery, National Cancer Center Hospital East, Chiba, Japan

²Division of Gastrointestinal Oncology, National Cancer Center Hospital East, Chiba, Japan

³Division of Esophageal Surgery, National Cancer Center Hospital, Tokyo, Japan

Correspondence

Takeo Fujita, Division of Esophageal Surgery, National Cancer Center Hospital East, 6-5-1 Kashiwanoha, Kashiwa, Chiba 277-8577, Japan.
Email: takfujit@east.ncc.go.jp

Abstract

Background: The first choice of an esophageal substitute after esophagectomy for cancer is the stomach. However, the colon must be considered for reconstruction in specific situations. The purpose of this study was to clarify the frequency and clinical features of patients who underwent colon interposition in thoracic esophagectomy and to investigate the postoperative complications and survival.

Methods: We conducted a retrospective case–control study in the National Cancer Center Hospital East, Japan. Patients who underwent colon interposition after esophagectomy for cancer between 2010 and 2020 were analyzed.

Results: Eighty-eight patients underwent esophagectomy with colon interposition; 53.2% received preoperative treatment and 52.3% underwent thoracoscopic surgery. Clavien–Dindo grade >III postoperative complications occurred in 42% of the patients; anastomotic leakage was the most common complication, occurring in 26.1% of the cases. Univariate analysis of the factors associated with Clavien–Dindo grade <III complications showed that the period 2015–2020 and totally mechanical Collard anastomosis were significant factors, with odds ratios (OR) of 0.264 and 0.267 ($p = 0.00327$ and $p = 0.00335$), respectively. Totally mechanical Collard anastomosis was associated with a lower risk of anastomotic leakage by univariate and multivariate analysis (OR, 0.257, $p = 0.00566$ and OR, 0.285, $p = 0.133$, respectively). Three-year overall survival was 54.2%. Univariate and multivariate analysis of overall survival showed that older age was a risk factor (OR, 1.08) for complications.

Conclusion: In colon reconstruction after esophageal cancer resection, totally mechanical Collard anastomosis for cervical anastomosis may reduce the risk of Clavien–Dindo grade >III complications.

KEYWORDS

anastomotic leak, cancer, colon, esophagectomy, surgical anastomosis

INTRODUCTION

The first colon interposition as a substitute after esophagectomy was reported by Kelling in 1911, and the first successful clinical colon interposition was performed by Von Hacker in 1914.¹ Later, in the first half of the 20th century, the colon became the “most commonly used reconstructive organ”.² However, in the latter half of the century, the stomach became the first choice for reconstruction after esophagectomy.³ In the modern era,

the first choice for an esophageal substitute is the stomach and the next is the ileocolon, if the stomach is unsuitable.^{4–8} However, in special situations, such as previous gastrectomy, extensive tumors in the stomach or esophagus, gastric tube cancer, or gastric tube necrosis or narrowing, the stomach cannot be used for reconstruction. In these situations, the best option is the colon.^{7,9–13}

Therefore, the purpose of this study was to analyze cases of colon reconstruction over an 11-year period from 2010 to

2020 at our hospital, which is one of the leading high-volume centers in Japan, and to clarify the frequency of postoperative complications and survival outcomes.

METHODS

Patients

This was a single-center retrospective case-control study performed in the Department of Esophageal Surgery, National Cancer Center Hospital East, Kashiwa, Japan. Patients who underwent colon reconstruction after esophagectomy for cancer between 2010 and 2020 were included in the study.

The primary endpoint was Clavien-Dindo grade >III postoperative complications.¹⁴ The secondary endpoint was overall survival and the details of complications, such as anastomosis leakage.

We reviewed the patients' medical records and collected data regarding their characteristics and surgical outcomes. The tumor stage was in accordance with the 8th edition of the Union for International Cancer Control (UICC).¹⁵ The classifications of cases early in the study period were converted to the 8th edition classification from the 7th edition or 6th edition. This retrospective study was approved by the Ethics Committee of the National Cancer Center East (2018-322).

Preoperative treatment

According to national guidelines, esophageal cancer patients with clinical (c) tumor (T) stage 1 and node (N)-positive (cT1 N+) or cT2-cT4 any N cancer received preoperative treatment.¹⁶

The docetaxel, cisplatin, and fluorouracil (DCF) regimen consisted of intravenous docetaxel 70 mg/m² and cisplatin 70 mg/m² on day 1 and a continuous infusion of 5-fluorouracil 750 mg/m²/day for 5 days. This regimen was repeated every 3 weeks until unacceptable toxicity, patient refusal, or disease progression, to a maximum of 3 cycles. Prophylactic use of granulocyte colony-stimulating factor was allowed, and prophylactic use of ciprofloxacin on days 5-15 was mandatory.¹⁷

The 5-fluorouracil and cisplatin (FP) regimen consisted of intravenous cisplatin 80 mg/m² on day 1 and a continuous infusion of 5-fluorouracil 1150 mg/m²/day for 5 days. This regimen was repeated every 3 weeks until unacceptable toxicity, patient refusal, or disease progression, to a maximum of 2 cycles.

The chemoradiotherapy (CRT) regimen consisted of 41.4 Gy radiotherapy plus 2 cycles of 5-fluorouracil/cisplatin, including cases where CRT was performed at a previous hospital.

Surgical approach

Esophageal subtotal resection was performed via right thoracotomy or right thoracoscopy, and mediastinoscopy was

used for high-risk patients. Thoracoscopic surgery is not hybrid approach open and video-assisted thoracic surgery (VATS), but complete thoracoscopic surgery. Mediastinoscopic approach is a method of esophageal resection by inserting a 5-mm camera, two surgeon's ports, and an assistant's port through the neck to perform esophageal feeding and lymph node dissection toward the ventral side, after that esophageal feeding and lymph node dissection through the esophageal fissure by laparoscopy, and traffic with feeding from the neck. The patient's position was in the left lateral decubitus position for open thoracotomy, prone position for thoracoscopy, and supine position for mediastinoscopy. Abdominal and cervical operations were then performed, with the abdominal operation being an open operation for colonic reconstruction. The reconstruction route was posterior to the sternum for thoracotomy and thoracoscopy and posterior mediastinal for mediastinoscopy.

The nasogastric tube (NG)-tube inserted intraoperatively for all patients from their nasal. The tip of the tube implanted across the cervical anastomosis for decompression. Standard three-field lymphadenectomy was performed systematically.

Colon interposition

Colon interposition was principally performed using the right colon, with the right branch of the middle colic artery as the main feeding artery. The ileocolonic artery was dissected or preserved on a case-by-case basis. The ileum on the oral side was left slightly longer for dissection, and the transverse colon on the anal side was dissected between the right and left branches of the middle colic artery. After elevation to the cervical area, the excess ileum was separated, and anastomosis of the residual esophagus and ileum was performed at the neck by hand sewing or with the totally mechanical Collard technique.¹⁸ The anal end of the ascending colon was anastomosed with the proximal jejunum using a circular stapler end-to-side, and the ileum was anastomosed with the transverse colon by functional end-to-end anastomosis.

Postoperative management

After surgery, patients were extubated in the operating room and returned to the intensive care unit (ICU). On the first postoperative day, a laryngoscope was used to check for antegrade nerve palsy by evaluating vocal cord movement. The patient was then weaned from ventilation and discharged from the ICU to return to the general ward. On the third postoperative day, tube feeding was started via enterostomy or nasal tube. On the seventh postoperative day, swallowing angiography was performed under fluoroscopy to identify abnormalities in the cervical anastomosis, such as leakage and stricture, and to evaluate the elevated colon and confirm smooth flow from the intestine. If there were no problems, the nasal decompression tube was removed and

oral intake was started. Gradually, the calories from oral intake were increased and calories from tube feeding were decreased. If the patient was judged sufficiently well, they were discharged home. All patients were re-evaluated for postoperative complications at the time of discharge and the Clavien–Dindo grade and complication details were recorded.

Definition of postoperative complications

Anastomotic leakage was defined as any clinical signs of a salivary fistula, confirmed by a water-soluble radiologic contrast swallow under fluoroscopy, or endoscopic visualization of dehiscence or fistula at the anastomosis site.

Anastomotic stricture was defined as dysphagia with some solids and requiring endoscopic balloon dilation, with stenosis.

Complication management

In the case of bilateral recurrent nerve palsy, a Mini-Trach II (Portex) was inserted through the cricothyroid ligament. If anastomotic leakage was observed, we opened the neck incision and inserted and positioned a decompression tube through the nasal passage. If treatment was ineffective, or if the case was severe, after opening the neck wound, we inserted a 10–12-Fr Salem Sump tube (Sherwood Medical Industries) from the incision into the area of anastomotic leakage and created an internal/external fistula. If anastomotic stenosis was found, we performed endoscopic or rigid bougie dilatation.

Statistical analysis

All data were analyzed using free software EZR (Satima Medical Center, Jichi Medical

University).¹⁹ Nominal variables were compared using Fisher's test, and continuous variables were analyzed using Student's *t*-test. When normality was not observed, the Mann–Whitney U test was used for comparisons. Univariate and multivariate analyses were performed using logistic regression analysis. Multivariate factors were chosen using the stepwise Akaike's information criterion (AIC) method. The log rank test with the Kaplan–Meier method was used to describe the survival curves and for comparisons. Cox hazard regression was used for multivariate analysis of survival, and cut-off values were determined using receiver operating characteristic (ROC) curves. Variables with $p < 0.05$ in the univariate analysis were included in the multivariate logistic regression model. Odds ratios (ORs) with 95% confidence intervals (CIs) were calculated, and $p < 0.05$ was considered statistically significant.

RESULTS

Between January 2010 and March 2020, 1561 patients underwent surgery at the Department of Esophageal Surgery, National Cancer Center Hospital East, Japan; 88 (5.6%) patients underwent esophageal reconstruction with colon interposition. We excluded patients who underwent cervical esophagectomy or total pharyngolaryngoesophagectomy (TPLE), even if colon reconstruction was performed (Figure 1). The patients' mean age was 70.7 years (± 7.91 standard deviation [SD]). The most common performance score (PS) was 0 (70.5%), and the mean body mass index (BMI) was 19.33 kg/m² (± 2.84 SD). The reason for colon reconstruction was post-gastrectomy in 72.7% of the patients, and tumors were located predominantly in the mid-thoracic/lower thoracic (Mt/Lt) regions: 44.3%/44.3%. According to the tumor-node-metastasis (TNM) classification (UICC 8th edition), the percentage of patients with stage 3/4 cancer was 45.5% (Table 1).

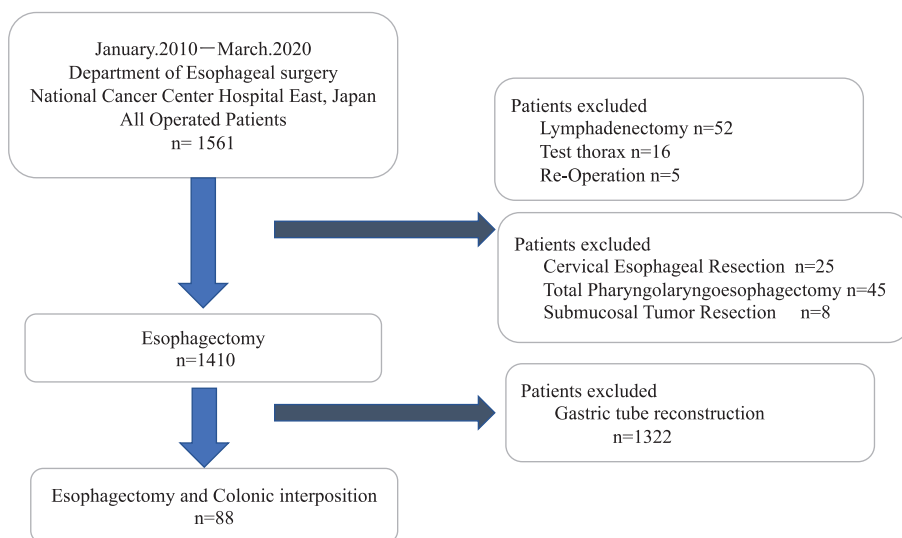


FIGURE 1 Patient selection diagram between January 2010 and March 2020, 1561 patients underwent surgery at the Department of Esophageal Surgery, National Cancer Center Hospital East, Japan; 88 (5.6%) patients underwent esophageal reconstruction with colon interposition. The excluded cases are shown on the right

Preoperative treatment was administered to 53.2% patients; 21.6% of these patients received DCF, which accounted for 40% of the patients receiving preoperative treatment. Basically, the treatment policy of our hospital is to provide preoperative treatment to patients with clinical (c) tumor (T) stage 1 and node (N)-positive (cT1 N+) or cT2–cT4 any N cancer, but there were patients who did not receive preoperative treatment based on their ages, general condition, renal function, and PS. Regarding the surgical approach, 52.3% of the patients underwent thoracoscopy. The most common route of reconstruction was retrosternal,

TABLE 1 Patients' characteristics

Variable	Value (n = 88)
Age, y (SD)	70.7 (7.91)
Male/female	82/6 (93.2/6.8%)
Performance status (0/1/2)	62/25/1 (70.5/28.4/1.1%)
Body mass index mean (SD) (kg/m ²)	19.33 (2.84)
Medical history	
Diabetes mellitus	14 (15.9%)
Hypertension	38 (43.2%)
Heart disease	12 (13.6%)
Other cancer	30 (34.1%)
Respiratory disease	10 (11.4%)
Gastric/duodenal ulcer	30 (34.1%)
Alcohol	74 (75%)
Tobacco	74 (77.5%)
Brinkman index (SD)	733.4 (510)
Reason for colon reconstruction	
Post-gastrectomy	65 (72.7%)
Complication of gastric cancer	21 (25.1%)
Gastric invasion	1 (1.1%)
Gastric conduit cancer	1 (1.1%)
Laboratory data	
Hb (SD) (g/L)	118 (17.0)
Alb (SD) (g/L)	39.1 (4.5)
Histological type (SCC /adenocarcinoma)	84/4 (95.5/4.6%)
Study period 2010–2014/2015–2020	40/48 (45.5%/54.5%)
Location (Ce/Ut/Mt/Lt)	1/7/39/39 (1.1/8.0/44.3/44.3%)
cT (1a/1b/2/3/4a/4b)	35/10/38/3/1 (39.7/11.4/43.2/3.3/1.1%)
cN (0/1/2/4)	38/24/21/5 (43.2/27.3/23.9/5.7%)
cM (0/1/1[104])	78/8/2 (88.6/9.3/2.2%)
cStage (I/II/III/IVA/IVB)	31/17/28/3/9 (35.2/19.3/31.8/3.4/10.2%)
cStage III/IV	40 (45.5%)

Note: Values are N (%) unless otherwise indicated.

Abbreviations: Alb, albumin; Ce, cervical; cM, clinical metastasis stage; cN, clinical node stage; cStage, cancer stage; cT, clinical tumor stage; Hb, hemoglobin; Lt, lower thoracic; Mt, mid-thoracic; SCC, squamous cell carcinoma; SD, standard deviation; Ut, upper thoracic.

TABLE 2 Details of the preoperative treatments and operations

Variable	Value (n = 88)
Preoperative treatment	47 (53.4)
None	41 (46.6)
DCF 1/2/3 cycles	3/2/14 (3.4/2.3/15.9)
FP 1/2 cycles	3/12 (3.4/13.6)
FOLFOX	1 (1.1)
TS-1	2 (2.3)
CRT	6 (6.8)
ESD	3 (3.4)
RT	1 (1.1)
Operation approach	
Thoracotomy	33 (37.5)
Thorascopic	46 (52.3)
Mediastinoscopic	9 (10.2)
Operation time, min	413.0 (270.2–476.0)
Total blood loss, g	268.5 (124.7–521.0)
Reconstruction route	
Retrosternal	76 (86)
Posterior mediastinal	9 (10)
Subcutaneous	3 (3.4)
Two-phase operation	23 (26.1)
Preserved ileocolic artery	34 (38.6)
Cervical anastomosis	
Totally mechanical collar	42 (47.7)
Hand-sewn	43 (48.9)
Circular stapler	3 (3.4)

Note: Values are N (%) or median (interquartile range).

Abbreviations: CRT, chemoradiotherapy regimen consisting of 41.4 Gy radiotherapy plus 2 cycles of 5-fluorouracil/cisplatin; DCF, docetaxel 70 mg/m² and cisplatin 70 mg/m² on day 1 and a continuous infusion of 5-fluorouracil 750 mg/m²/day for 5 days; ESD, endoscopic submucosal dissection; FOLFOX, oxaliplatin 85 mg/m², levofolinate calcium 200 mg/m², and 5-fluorouracil 400 mg/m² on day 1 and a continuous infusion of 5-fluorouracil 2400 mg/m²/day for 2 days; FP, cisplatin 80 mg/m² on day 1 and a continuous infusion of 5-fluorouracil 1150 mg/m²/day for 5 days; RT, radiotherapy.

TABLE 3 Complications and postoperative hospital stay

Variable	Value (n = 88)
Clavien–Dindo grade ≤III	37 (42)
Anastomotic leakage	23 (26.1)
Anastomotic stenosis	10 (11.3)
Respiratory complication	14 (15.9)
Chylothorax	1 (1.1)
Ileus	6 (6.8)
Necrosis of the elevated intestine	1 (1.1)
Clavien–Dindo grade ≥II	7 (8.0)
Postoperative hospital stay	22.0 (16–31)
In-hospital death	4 (4.5)

Note: Values are N (%) or median (interquartile range).

at 86%. Because of the high risk of leakage in colon reconstruction, the posterior mediastinal route can lead to mediastinitis and other serious complications if leakage occurs in

the cervical anastomosis. Preservation of the ileocolic artery was performed in 38.6% of the patients. The cervical anastomosis was hand sewn in 48.9% of the patients compared

TABLE 4 Univariate and multivariate analysis of Clavien–Dindo grade \leq III complications

	OR	Univariate analysis 95% CI	<i>p</i> value	OR	Multivariate analysis 95% CI	<i>p</i> value
Patient background factors						
Age, y	1.030	0.972–1.08	0.353			
Body mass index	0.925	0.796–1.07	0.308			
Performance status	1.63	0.677–3.93	0.275			
Study period: 2015–2020	0.264	0.109–0.641	0.00327	0.604	0.100–3.65	0.583
Hb	1.030	0.803–1.32	0.825			
Alb	0.782	0.309–1.98	0.604			
Stage III/IV cancer	0.692	0.298–1.61	0.392			
Surgical factors						
Preoperative treatment	0.434	0.184–1.02	0.0562	0.631	0.244–1.63	0.3410
Thoracotomy	1.63	0.682–3.89	0.272			
Thoracoscopy	0.577	0.248–1.34	0.202			
Two-phase operation	1.810	0.689–4.78	0.228			
Preserved ileocolic artery	1.21	0.513–2.86	0.662			
Totally mechanical collard anastomosis	0.267	0.11–0.645	0.00335	0.464	0.0816–2.64	0.387
Hand sewn anastomosis	2.78	1.17–6.59	0.0203			

Abbreviations: Alb, albumin; CI, confidence interval; Hb, hemoglobin; OR, odds ratio.

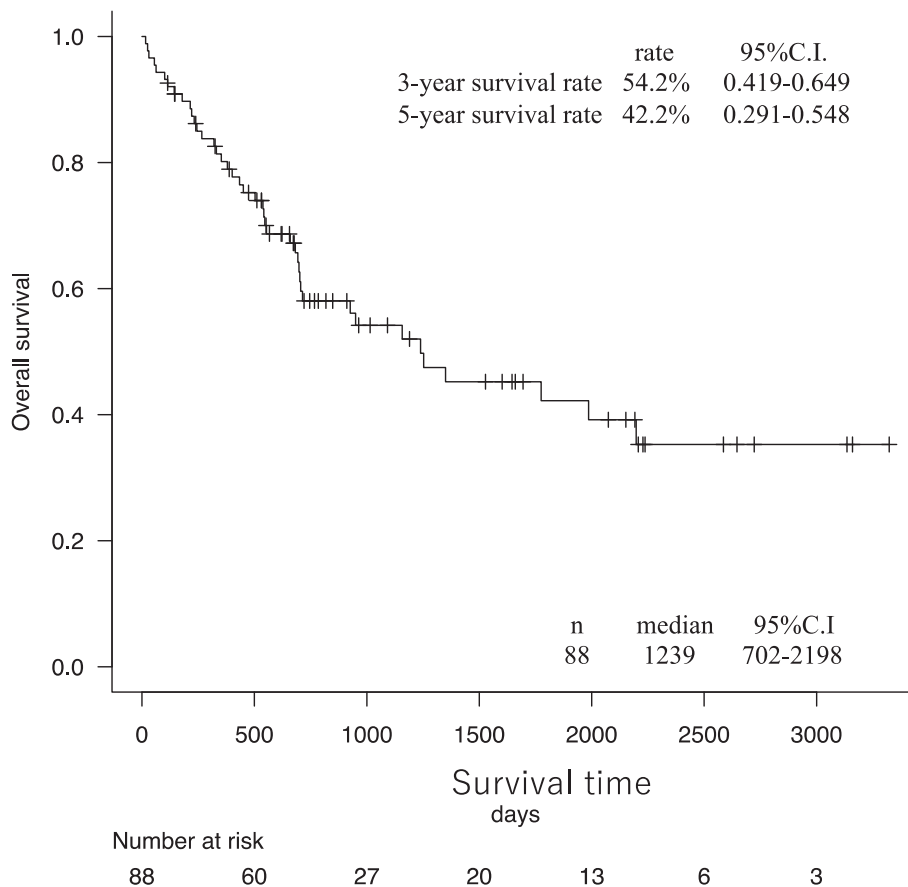


FIGURE 2 Overall survival of all patients who underwent colon interposition. The 3-year survival rate was 54.2%, and the 5-year survival rate was 42.2%. The median overall survival was 1239 days. CI, confidence interval

with the totally mechanical Collard method in 47.7% of the patients; anastomosis was performed with a circular stapler in only 3.4% of the patients (Table 2).

Clavien–Dindo grade >III postoperative complications were observed in 37% of the patients; anastomotic leakage was the most common complication at 26.1%. Respiratory complications were observed in 15.9% of the patients, and these comprised pneumonia, pneumothorax, pyothorax, and sputum aspiration during bronchoscopy. Necrosis of the elevated intestine was observed in only one case, and in-hospital death occurred in four cases (Table 3). There was one case of bilateral recurrent nerve palsy. There are three cases of leakage from distal anastomosis. In Table S1, totally mechanical Collard anastomosis was 9.5% leakage in cervical anastomosis. All cases were R0 resections, and there were no positive resection margins. (Table S2).

Univariate analysis of the risk factors for Clavien–Dindo grade >III complications showed that the study period 2015–2020, totally mechanical Collard anastomosis and hand sewn anastomosis were statistically significant risk factors, with ORs of 0.264, 0.267, and 2.78, respectively. Neither preoperative treatment nor thoracoscopy reduced the OR (OR, 0.434 and OR, 0.5777, respectively). Two-phase operation increased the risk of Clavien–Dindo grade >III complications, with an OR of 1.810. Factors included in the multivariate analysis were the period 2015–2020, preoperative treatment, and totally mechanical Collard anastomosis, using the stepwise AIC method. Totally mechanical Collard anastomosis had an OR of 0.464 (Table 4). In Table S3, totally mechanical Collard anastomosis was also associated with a decreased risk of anastomotic leakage by univariate and multivariate analysis (OR, 0.257, $p = 0.00566$ and OR, 0.285, $p = 0.133$, respectively).

Overall survival data are shown in Figure 2; the 3-year survival rate was 54.2%, and the 5-year survival rate was 42.2%. The median survival time was 1239 days (Figure 2).

Univariate analysis of overall survival showed statistically significant differences for age as a risk factor for higher risk of developing complications (OR, 1.07, $p = 0.0014$) and thoracoscopy as a factor associated with a decreased risk of developing complications (OR, 0.478, $p = 0.0205$). cStage 3/4 (OR, 1.73) and Clavien–Dindo grade >III (OR, 1.83) complications were associated with lower survival. In the multivariate analysis, age was a risk factor for lower overall

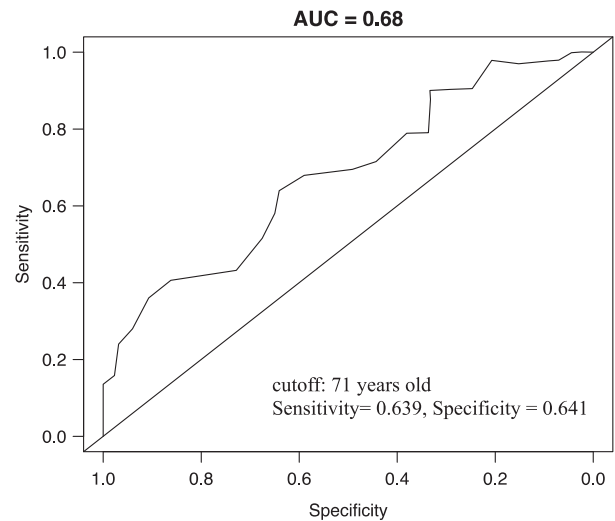


FIGURE 3 ROC curve of age for overall survival. We evaluated survival time at 1239 days (median overall survival); the AUC was 0.68. The ROC cut-off value was 71 years, for overall survival, with a sensitivity and specificity of 0.639 and 0.641, respectively. AUC, area under the curve; ROC, receiver operating characteristic

TABLE 5 Univariate and multivariate analysis of overall survival

	HR	Univariate analysis 95% CI	<i>p</i> value	HR	Multivariate analysis 95% CI	<i>p</i> value
Patient background factors						
Age, y	1.077	1.029–1.127	0.0014	1.08	1.039–1.14	0.00035
Body mass index	0.904	0.777–1.05	0.192			
Performance status	2.260	0.920–5.57	0.075			
Hb	0.846	0.655–1.09	0.200	0.80	0.671–1.154	0.13
Alb	0.387	0.145–1.04	0.0586			
Stage III /IV	1.736	0.939–3.207	0.0781	1.704	0.914–3.176	0.093
Study period: 2015–2020	0.7576	0.401–1.432	0.3926			
Surgical factors						
Preoperative treatment	0.749	0.406–1.383	0.356			
Thoracotomy	1.65	0.8994–3.051	0.1053			
Thoracoscopy	0.478	0.2565–0.8925	0.0205			
Two-phase operation	1.428	0.7418–2.748	0.2864			
Clavien–Dindo grade ≥III	1.836	0.9744–3.459	0.0601	1.739	0.913–3.31	0.0918
Clavien–Dindo grade ≤II	1.715	0.7205–4.082	0.2228			

Abbreviations: Alb, albumin; CI, confidence interval; Hb, hemoglobin; HR, hazard ratio.

survival (OR, 1.08, $p = 0.00035$) (Table 5). Therefore, we determined the cut-off value for age (71 years) using a ROC curve analysis. (Figure 3).

DISCUSSION

In recent decades, indications for colon interposition have declined because the use of gastric tubes has become more acceptable as a first-line option for esophagectomy in cancer patients.²⁰ In the most recent series, rates of colon interposition for cancer were $<10\%$.^{9–13,21} In the literature, the most common reason for colorectal implantation in cancer patients was a history of gastrectomy.^{9–12,21} In our study, a history of gastrectomy was also the most common reason (80%); complications related to gastric cancer was the next most common reason (25.1%), followed by gastric invasion or gastric conduit cancer (GCC). The estimated incidence of GCC after esophagectomy is 0.2%–5.7%, and GCC prevails in Asian patients.^{22,23} Although gastric tube reconstruction is the most common reconstruction method after esophageal cancer surgery,^{4–7} colon reconstruction will not disappear, for the reasons mentioned. It is difficult to study postoperative complications and the associated risk factors following colon interposition owing to the small number of cases^{24,25}; however, in this study, we analyzed the largest number of cancer patients in the last 10 years. Furthermore, trends were seen when we evaluated the short-term results of recent cases compared with all cases over the 11 years of the study.

First, one difference compared with the systematic review by Brown et al.²⁵ published in 2016 is the use of the right colon and the retrosternal pathway. In the systematic review, the use of the left colon and posterior mediastinal reconstruction were the most common.²⁵ Additionally, the method of cervical anastomosis changed over time, during our study with hand sewn anastomosis accounting for 92.5% of anastomoses from 2010 to 2014 (early group), whereas the totally mechanical Collard anastomosis accounted for 87.5%, and hand sewn anastomosis decreased to 12.5% from 2015 to 2020 (late group) (Table S4). This was a very significant change over time. Hand sewn anastomosis is widely used, with leakage rates of 0%–33% and stenosis rates of 2%–89% for this method.²⁶ Linear stapled cervical semi-mechanical anastomosis was first described by Collard.²⁷ Orringer et al.²⁸ reported a Collard method in which the posterior esophageal wall is anastomosed not to the posterior wall, but to the anterior wall of the gastric conduit (overlap method). Both the functional end-to-end Collard technique and the Orringer modified overlap Collard technique reduce the frequency of strictures compared with the hand sewn technique.^{28,29} Another variation of the modified Collard technique is totally mechanical anastomosis, which is a posterior-to-posterior linear and transverse stapled (functional end-to-end) method.¹⁸ Since December 2014, our hospital has used the totally mechanical Collard technique for anastomosis owing to concerns about the

relatively high rate of anastomotic stenosis, and there was a similar trend in colon reconstruction.

Second, regarding postoperative complications, 42% of the patients in this study developed Clavien–Dindo grade $>III$ complications (Table 4). This may seem like a large number, but observation over time showed that the rate was 67.5% from 2010–2014 and decreased to 10.8% in the last 6 years (Table S5). We actively use bronchoscopic sputum aspiration to prevent pneumonia and to prevent pneumonia from becoming serious, which may be one of the reasons why the Clavien–Dindo grade $>III$ complications were so high. Anastomotic leakage was observed in a high percentage (26.1%) of patients (Table 4). However, the rate was 78% from 2010–2014, and had declined since 2015. This was thought to be related to the change in anastomosis method to the Totally Mechanical Collard anastomosis. It has been shown in previous articles^{30–32} that major complications decrease as the number of experienced surgeons increases. The fact that anastomotic leakage has decreased in the late group (2015–2020) at our hospital suggests that the technique and method have become more proficient. In the univariate analysis of Clavien–Dindo grade $>III$ complications, the period 2015–2020 had an OR of 0.264 ($p = 0.0032$), which supports the above findings. When multivariate analysis was performed for the period 2015–2020, preoperative treatment, and totally mechanical Collard anastomosis, the risk of developing complications tended to decrease in the late group, with an OR of 0.604. When the analysis was limited to anastomotic leakage, the period 2015–2020, totally mechanical Collard anastomosis, and hand sewing were risk factors in the univariate analysis, with ORs of 0.329 and 0.257 for the period 2015–2020 and totally mechanical Collard anastomosis, respectively, which lowered the risk of anastomosis leakage. In contrast, hand sewn anastomosis had an OR of 3.82, which was associated with an increased risk of anastomotic leakage. All of these findings could be associated with the same factor, as totally mechanical Collard anastomosis increased significantly from 2015–2020, and hand sewing decreased significantly. Therefore, in the multivariate analysis, we removed the factors, the period from 2015–2020 and hand sewn anastomosis and examined the factors. The OR for totally mechanical Collard anastomosis was 2.85 ($p = 0.0133$), and this factor was also associated with a lower risk of anastomotic leakage (Table S3). Totally mechanical Collard anastomosis may reduce the risk of anastomotic leakage of the cervical anastomosis in colon reconstruction.

Third, univariate analysis of overall survival showed a statistically significant difference for age as a risk factor for increased complications (OR, 1.07, $p = 0.0014$) and thoracoscopy as a factor associated with decreased risk (OR, 0.478, $p = 0.0205$). In addition, cStage 3/4 and Clavien–Dindo grade $>III$ complications were common, with ORs of 1.73 and 1.83, respectively (Table 5). Multivariate analysis showed that age was also a risk factor, with a cutoff value of 71 years (Table 5, Figure 3).

Recently, at our hospital, preoperative treatment for colon reconstruction after esophagectomy, especially induction DCF and the increased use of totally mechanical Collard anastomosis, has tended to reduce the number of serious complications (Clavien–Dindo grade >III) and anastomotic leakage cases. Regarding anastomotic leakage changing to the totally mechanical Collard anastomosis appears to have the potential to reduce the risk of complications.

The limitations of this study were the single-center, retrospective, case–control design, and that the surgical technique and preoperative treatment changed over the study period. However, the strength of our study is that the postoperative management was based on a clinical pathway, which was consistent. Another strength is that we experienced 88 cases of colon reconstruction in 11 years, which is difficult to collect.

In conclusion, in colon interposition after esophageal cancer resection, totally mechanical Collard anastomosis for cervical anastomosis and preoperative treatment may reduce the risk of Clavien–Dindo grade >III complications.

ACKNOWLEDGMENTS

We greatly appreciate the members of the Division of Esophageal Surgery for their critical discussion of our manuscript. We thank the members of the Division of Anesthesiology for reviewing and discussing the study. We thank Jane Charbonneau, DVM, from Edanz (<https://jp.edanz.com/ac>) for editing a draft of this manuscript.

CONFLICT OF INTEREST

Authors declare no conflict of interests for this article.

DATA ACCESSIBILITY STATEMENT

Other researchers can use the original data if they send us an email and explain that they want to use the original data. Because the original data for this study is from within our facility, it cannot be obtained from outside sources.

ORCID

Takeo Fujita  <https://orcid.org/0000-0002-6098-9813>

REFERENCES

- Lee K, Kim HR, Park S i, Kim DK, Kim YH, Choi SH. Surgical outcome of colon interposition in esophageal cancer surgery: analysis of risk factors for conduit-related morbidity. *J Thorac Cardiovasc Surg.* 2017;66(5):384–9. <https://doi.org/10.1055/s-0037-1606828>
- May IA, Samson PC. Esophageal reconstruction and replacements. *Ann Thorac Surg.* 1969;7(3):249–77. [https://doi.org/10.1016/S0003-4975\(10\)66183-8](https://doi.org/10.1016/S0003-4975(10)66183-8)
- Akiyama H, Miyazono H, Tsurumaru M. Use of the stomach as an esophageal substitute. *Ann Surg.* 1978;188(1):606–10.
- David B. Esophageal reconstruction. *Am J Surg.* 1980;139(1):810–4.
- Maish MS, DeMeester SR. Indications and technique of colon and jejunal interpositions for esophageal disease. *Surg Clin North Am.* 2005;85(3):505–14. <https://doi.org/10.1016/j.suc.2005.01.014>
- Hüttl TP, Wichmann MW, Geiger TK, Schildberg FW, Fürst H. Techniques and results of esophageal cancer surgery in Germany. *Langenbecks Arch Surg.* 2002;387(3–4):125–9. <https://doi.org/10.1007/s00423-002-0294-x>
- Davis PA, Law S, Wong J. Colonic interposition after esophagectomy for cancer. *Arch Surg.* 2003;138(3):303–8. <https://doi.org/10.1001/archsurg.138.3.303>
- Kawano T, Nishikage T, Kawada K, Nakajima Y, Kojima K, Nagai K. Subcutaneous reconstruction using ileocolon with preserved ileocolic vessels following esophagectomy or in esophageal bypass operation. *Dig Surg.* 2009;26(3):200–4. <https://doi.org/10.1159/000217799>
- Klink CD, Binnebösel M, Schneider M, Ophoff K, Schumpelick V, Jansen M. Operative outcome of colon interposition in the treatment of esophageal cancer: a 20-year experience. *Surgery.* 2010;147(4):491–6. <https://doi.org/10.1016/j.surg.2009.10.045>
- Hamai Y, Hihara J, Emi M, Aoki Y, Okada M. Esophageal reconstruction using the terminal ileum and right colon in esophageal cancer surgery. *Surg Today.* 2012;42(4):342–50. <https://doi.org/10.1007/s00595-011-0103-7>
- Mine S, Udagawa H, Tsutsumi K, Kinoshita Y, Ueno M, Ehara K, et al. Colon interposition after esophagectomy with extended lymphadenectomy for esophageal cancer. *Ann Thorac Surg.* 2009;88(5):1647–53. <https://doi.org/10.1016/j.athoracsur.2009.05.081>
- Saeki H, Morita M, Harada N, Egashira A, Oki E, Uchiyama H, et al. Esophageal replacement by colon interposition with microvascular surgery for patients with thoracic esophageal cancer: the utility of superdrainage. *Dis Esophagus.* 2013;26(1):50–6. <https://doi.org/10.1111/j.1442-2050.2012.01327.x>
- Reslinger V, Tranchart H, D'Annunzio E, Poghosyan T, Quero L, Munoz-Bongrand N, et al. Esophageal reconstruction by colon interposition after esophagectomy for cancer analysis of current indications, operative outcomes, and long-term survival. *J Surg Oncol.* 2016;113(2):159–64. <https://doi.org/10.1002/jso.24118>
- Dindo D, Demartines N, Clavien PA. Classification of surgical complications: a new proposal with evaluation in a cohort of 6336 patients and results of a survey. *Ann Surg.* 2004;240(2):205–13. <https://doi.org/10.1097/01.sla.0000133083.54934.ae>
- Brierley J, Gospodarowicz MD, Wittekind C. Union for International Cancer Control. TNM classification of malignant tumors. West Sussex, UK: Wiley Blackwell; 2017.
- Kitagawa Y, Uno T, Oyama T, Kato K, Kato H, Kawakubo H, et al. Esophageal cancer practice guidelines 2017 edited by the Japan esophageal society: part 2. *Esophagus.* 2019;16(1):25–43. <https://doi.org/10.1007/s10388-018-0642-8>
- Shinoda M, Ando N, Kato K, Ishikura S, Kato H, Tsubosa Y, et al. Randomized study of low-dose versus standard-dose chemoradiotherapy for unresectable esophageal squamous cell carcinoma (JCOG0303). *Cancer Sci.* 2015;106(4):407–12. <https://doi.org/10.1111/cas.12622>
- de Giacomo T, Francioni F, Venuta F, Trentino P, Moretti M, Rendina EA, et al. Complete mechanical cervical anastomosis using a narrow gastric tube after esophagectomy for cancer. *Eur J Cardiothorac Surg.* 2004;26(5):881–4. <https://doi.org/10.1016/j.ejcts.2004.07.024>
- Kanda Y. Investigation of the freely available easy-to-use software “EZR” for medical statistics. *Bone Marrow Transplant.* 2013;48(3):452–8. <https://doi.org/10.1038/bmt.2012.244>
- Nederlof N, Tilanus HW, Tran TCK, Hop WCJ, Wijnhoven BPL, de Jonge J. End-to-end versus end-to-side esophagogastronomy after esophageal cancer resection: a prospective randomized study. *Ann Surg.* 2011;254(2):226–33. <https://doi.org/10.1097/SLA.0b013e31822676a9>
- Motoyama S, Kitamura M, Saito R, Maruyama K, Sato Y, Hayashi K, et al. Surgical outcome of colon interposition by the posterior mediastinal route for thoracic esophageal cancer. *Ann Thorac Surg.* 2007;83(4):1273–8. <https://doi.org/10.1016/j.athoracsur.2006.11.049>
- Sugiura T, Kato H, Tachimori Y, Igaki H, Yamaguchi H, Nakanishi Y. Second primary carcinoma in the gastric tube constructed as an esophageal substitute after esophagectomy. *J Am Coll Surg.* 2002;194(5):578–83. [https://doi.org/10.1016/s1072-7515\(02\)01135-3](https://doi.org/10.1016/s1072-7515(02)01135-3)
- Lee GD, Kim YH, Choi SH, Kim HR, Kim DK, Park SL. Gastric conduit cancer after oesophagectomy for oesophageal cancer: incidence

- and clinical implications. *Eur J Cardiothorac Surg*. 2014;45(5):899–903. <https://doi.org/10.1093/ejcts/ezt497>
24. Fearon NM, Mohan HM, Fanning M, Ravi N, Reynolds JV. Colonic interposition, a contemporary experience: technical aspects and outcomes. *Updates Surg*. 2021;73(5):1849–55. <https://doi.org/10.1007/s13304-020-00920-5>
 25. Brown J, Lewis WG, Foliaki A, Clark GWB, Blackshaw GRJC, Chan DSY. Colonic interposition after adult oesophagectomy: systematic review and meta-analysis of conduit choice and outcome. *J Gastrointest Surg*. 2018;22(6):1104–11. <https://doi.org/10.1007/s11605-018-3735-8>
 26. Deng XF, Liu QX, Zhou D, Min JX, Dai JG. Hand-sewn vs linearly stapled esophagogastric anastomosis for esophageal cancer: a meta-analysis. *World J Gastroenterol*. 2015;21(15):4757–64. <https://doi.org/10.3748/wjg.v21.i15.4757>
 27. Collard JM, Romagnoli R, Goncette L, Otte JB, Kestens PJ. Terminalized semimechanical side-to-side suture technique for cervical esophagogastric anastomosis. *Ann Thorac Surg*. 1998;65(3):814–7. [https://doi.org/10.1016/S0003-4975\(97\)01384-2](https://doi.org/10.1016/S0003-4975(97)01384-2)
 28. Orringer MB, Marshall B, Iannettoni MD. Eliminating the cervical esophagogastric anastomotic leak with a side-to-side stapled anastomosis. *J Thorac Cardiovasc Surg*. 2000;119:277–88.
 29. Ercan S, Rice TW, Murthy SC, Rybicki LA, Blackstone EH. Does esophagogastric anastomotic technique influence the outcome of patients with esophageal cancer? *J Thorac Cardiovasc Surg*. 2005;129(3):623–31. <https://doi.org/10.1016/j.jtcvs.2004.08.024>
 30. Lerut T. The surgeon as a prognostic factor. *Ann Surg*. 2000;232(6):729–32.
 31. Migliore M, Choong CK, Lim E, Goldsmith KA, Ritchie A, Wells FC. A surgeon's case volume of oesophagectomy for cancer strongly influences the operative mortality rate. *Eur J Cardiothorac Surg*. 2007;32(2):375–80. <https://doi.org/10.1016/j.ejcts.2007.04.014>
 32. Yang Y, Li B, Hua R, Zhang X, Jiang H, Sun Y, et al. Assessment of quality outcomes and learning curve for robot-assisted minimally invasive McKeown esophagectomy. *Ann Surg Oncol*. 2021;28(2):676–84. <https://doi.org/10.1245/s10434-020-08857-0>

SUPPORTING INFORMATION

Additional supporting information may be found in the online version of the article at the publisher's website.

How to cite this article: Akutsu T, Fujita T, Kajiyama D, Ozaki A, Sato K, Fujiwara H, et al. Operative outcomes and long-term survival of patients undergoing colon interposition after esophagectomy for cancer. *Thorac Cancer*. 2022;13: 844–52. <https://doi.org/10.1111/1759-7714.14332>