

## Can intraoperative endoscopy prevent esophagojejunal anastomotic leakage after total gastrectomy?

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### Abstract

**Background:** Esophagojejunostomy (EJ) is frequently performed after total gastrectomy for proximal gastric tumors. Despite evolving surgical techniques and improving perioperative care, the EJ leak is one of the most severe life-threatening complications. This study investigated the preventability of postoperative anastomotic complications by performing intraoperative endoscopy.

**Methods:** We included 86 patients who underwent total gastrectomy and Roux-en-Y esophagojejunostomy anastomosis in the study. Patients were divided into two groups and analyzed retrospectively. Group 1 consisted of 43 patients who did not undergo intraoperative endoscopy between 2017 and 2019, and Group 2 included 43 patients who underwent intraoperative endoscopy between 2019 and 2020.

**Results:** Esophagojejunostomy anastomotic leak (EAL) was observed in 2.3 % of patients in Group 1 but not in Group 2. Anastomosis-related abnormal findings (anastomotic defect, bleeding, air leak, mucosal separation) were recorded in seven patients of Group 2 during endoscopy. When such findings were observed, additional full-thickness sutures were placed on the anastomosis line and strengthened. Complication related to anastomosis was not observed in the postoperative period in Group 2.

**Discussion:** After a total gastrectomy, the most severe complication affecting mortality, morbidity, and consequently the cost of the disease is esophagojejunal anastomotic leakage. Most of these complications are induced by technical errors not noticed during surgery. The crucial advantage of performing intraoperative endoscopy is the technically detailed evaluation of anastomosis.

**Conclusion:** Intraoperative endoscopy is a safe method to evaluate the strength of anastomosis. This procedure provides detailed information regarding anastomotic integrity. HIPPOKRATIA 2021, 25 (3):108-112.

**Keywords:** Perioperative endoscopy, gastric cancer, total gastrectomy, esophagojejunostomy, anastomotic leakage

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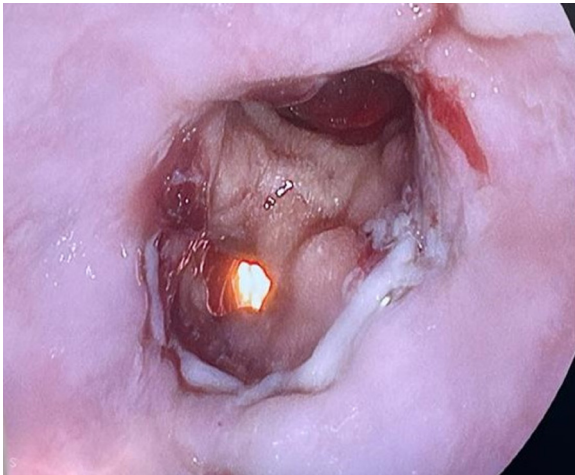
### Introduction

Gastric cancer is currently the fifth most common malignancy and the world's third leading cause of cancer-related deaths among all cancers<sup>1</sup>. Curative treatment in gastric cancer is surgical resection and adequate lymph node dissection<sup>2</sup>.

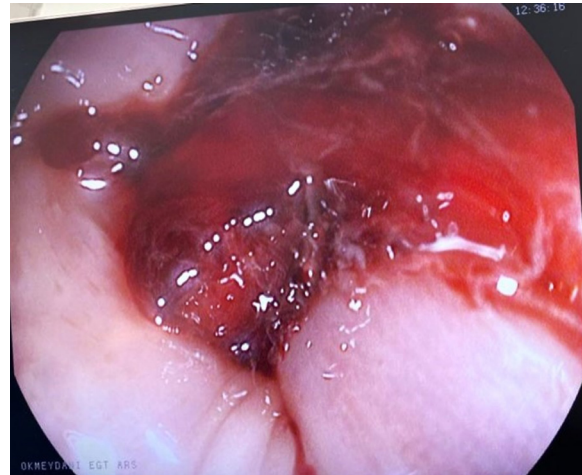
Although subtotal resection is sufficient for distal gastric cancers, total gastrectomy is required in proximal gastric cancers. Esophagojejunostomy anastomotic leak (EAL) after total gastrectomy is one of the most severe, life-threatening surgical complications<sup>3</sup>. Despite the development of surgical techniques, surgical instruments (stapler, etc.), and perioperative care, EAL rates after gastric cancer surgery have been reported to be 2.1 % to 14.7 %<sup>3-6</sup>. The presence of EAL increases mortality and morbidity and negatively affects the prognosis. It prolongs the length of hospital stay and causes an increase in patient care costs<sup>3,7,8</sup>.

The most important concern of surgeons after gastric resection is the safety of esophagojejunostomy (EJ) anastomosis. None of the tests performed to evaluate the integrity of the anastomosis, like the air leak test, methylene blue leak test, and integrity of stapler rings is entirely safe<sup>9,10</sup>. Intraoperative endoscopy (IOE) provides a more detailed examination of the anastomosis (Figure 1). Anastomotic integrity, air leak, bleeding, and anastomotic stenosis are evaluated with IOE (Figure 2), and any problem detected during endoscopy can be corrected during the procedure.

IOE is widely used in colorectal and bariatric surgery<sup>11-16</sup>. Limited studies evaluate the safety and durability of the anastomosis with IOE after gastric cancer surgery<sup>17-19</sup>. Our aim in this study was to investigate the safety of the IOE procedure and its impact on postoperative anastomosis-related complications.



**Figure 1:** Intraoperative endoscopy image showing anastomotic integrity.



**Figure 2:** Intraoperative endoscopy image showing bleeding at the site of the anastomosis.

## Methods

Ethical approval was obtained from the University of Health Sciences Okmeydanı Training and Research Hospital ethics committee in 2020. Eighty-six patients who underwent total gastrectomy Roux-en-Y esophagojejunostomy anastomosis for gastric cancer between July 2017 and September 2020 at Cemil Taşçıoğlu City Hospital General Surgery Clinic were analyzed retrospectively. Patients were divided into two groups. Group 1 consisted of 43 patients operated on between July 2017 and July 2019 who did not have IOE. Group 2 consisted of 43 patients operated on between July 2019 and September 2020 who had IOE. All patients included in the study were diagnosed with proximal gastric adenocarcinoma. All patients underwent curative intent total gastrectomy and D2 lymph node dissection performed by the same surgical team. EJ anastomoses were performed as an end-to-side Roux-en-Y esophagojejunostomy with a circular stapler (ILS 25 mm Ethicon endosurgery Inc., USA; and ILS 28 mm Covidien, USA).

In the IOE group, after completion of the anastomosis, the distal jejunal part was clamped. The operation field was filled with saline, with the remaining anastomosis in water. A gastroscope was inserted from the mouth, and the anastomosis was visualized. The air-water test was performed by insufflating air. The anastomosis was evaluated under direct vision for bleeding, stenosis, anastomotic and mucosal integrity.

Once an abnormal finding was detected (air leak, mucosal bleeding, mucosal detachment), additional full-thickness sutures (3/0 vicryl) or endoscopic intervention to the bleeding (cautery, injection, etc.) was performed. The effectiveness of the intervention was controlled by repeating endoscopy after the procedure. No additional procedure was required for patients with normal endoscopic findings.

Postoperative hospital stay, complications related to the anastomosis, and all complications, including re-

operation, were analyzed. Postoperative complications were classified according to Clavien-Dindo (CD)<sup>20</sup>. CD 1-2 was considered mild, while three and above as severe complications. Tumor staging was done according to TNM 8<sup>th</sup> edition<sup>21</sup>.

## Statistical Analysis

We used for statistical analyses the SPSS Statistics for Windows, Version 18.0. (SPSS Inc. Chicago, IL, USA). Continuous variables are expressed as mean  $\pm$  standard deviation. We compared the postoperative complications among groups using the Chi-square test and means using the Mann-Whitney U test. All tests are 2-sided, and we assessed statistical significance at a  $p < 0.05$  level.

## Results

Patients' demographic findings are shown in Table 1. The mean age, gender distribution, body mass index (BMI), comorbidities, operation times, and pathological stages of the two groups were similar ( $p > 0.05$ ). The most common comorbidities among patients were hypertension, diabetes mellitus, and chronic obstructive pulmonary disease. The distribution of patients who received neoadjuvant therapy was similar. There was no significant difference present between groups according to pathological TNM staging. Mean operation time didn't show a significant difference between the two groups.

Postoperative complications are shown in Table 2. Three of four patients with severe complications, according to CD, were in the group of non-IOE. Two of these were intra-abdominal bleeding, one was an anastomotic leak, and the other was a pancreatic fistula. There was no significant difference present between the two groups concerning general complications. In one of two patients with intra-abdominal bleeding, bleeding was controlled with re-operation, while blood transfusion was performed to the other without additional surgical procedures. One patient with an anastomotic leak was re-operated due to

**Table 1:** Demographic findings of the 86 patients included in the study, who underwent total gastrectomy and Roux-en-Y esophagojejunostomy anastomosis with (Group 2) or without (Group 1) intraoperative endoscopy.

Features	Group I (n =43)	Group II (n =43)	p
Age (years)	60.1 (29-83)	63.1 (39-89)	0.280
Gender (female/male)	13/30	13/30	1.000
BMI (kg/m <sup>2</sup> )	25.69	26.46	0.293
Comorbidity	26 (60.5 %)	19 (44.2 %)	0.195
Additional organ resection	7 (15.1 %)	7 (14.0 %)	1.000
Operation time (minutes)	256.44 (150-400)	240.69 (120-360)	0.209
Neoadjuvant treatment	32 (74 %)	27 (62.8 %)	0.353
T Stage			
EGC	5	6	1.00
AGC	38	37	
N Stage			
N 0**	16	18	0.826
N 1***	27	25	
M Stage*			
	2	1	1.000
TNM			
I	11	11	1.000
II	10	15	
III	20	16	
IV	2	1	

Values are given as means and range in brackets, or number of cases and percentage in brackets. n: number, BMI: Body Mass Index, EGC: Early Gastric Cancer, AGC: Advanced Gastric Cancer; TNM: stage as defined by Tumor, Node, Metastasis, \*: Positive peritoneal cytology is classified as a metastatic disease (M1), \*\*: Patients without lymph node metastases, \*\*\*: Patients with lymph node metastases.

**Table 2:** Postoperative complications of the 86 patients included in the study, who underwent total gastrectomy and Roux-en-Y esophagojejunostomy anastomosis with (Group 2) or without (Group 1) intraoperative endoscopy.

Features	Group I (n =43)	Group II (n =43)	p
Superficial surgical site infection	13 (30.2 %)	3 (7 %)	<b>0.011</b>
Complications according to CD			
Mild (CD <3)	18 (41.9%)	15 (34.9 %)	0.26
Severe (CD ≥3)	3 (7 %)	1 (2.3 %)	0.616
Anastomosis related complications			
Anastomotic leak	1 (2.3 %)	0	
Anastomotic bleeding	0	0	
Anastomotic stenosis	0	0	
Re-operation	1 (2.3%)	0	1.00
Length of hospital stay (days)	12.6 (6-152)	8.6 (6-16)	0.964

Values are given as number of cases and percentage in brackets, or means and range in brackets, n: number, CD: Clavien-Dindo classification.

abdominal sepsis, while the patient with a pancreatic fistula recovered with conservative treatment.

Postoperative severe complications were observed in three (7 %) patients in the non-IOE group while in one (2.3 %) patient in the IOE group ( $p=0.616$ ). The most common complication recorded in the patients was superficial surgical site infection. Superficial surgical site infection was more common in the group without IOE ( $p=0.011$ ). Regarding the length of hospital stay, there was no significant difference between the two groups ( $p=0.964$ ). No postoperative mortality was recorded in any group.

Doughnut control was evaluated as normal in both groups. IOE detected abnormal findings that would negatively affect the anastomosis in seven patients. Of these, two patients had air leaks, four had mucosal bleeding, and one had mucosal detachment. Abnormal findings were controlled by suture ligation in four and endoscopic intervention in three of these seven patients. The mean duration of the IOE was eight minutes in patients with normal findings and 16 minutes in patients with abnormal findings with additional intervention. No postoperative complications were seen after the additional intervention. The clinical course of these intervened patients is shown in Table 3.

### Discussion

Among the complications of anastomosis (intraluminal bleeding, leakage, anastomotic stricture), the most severe complication affecting mortality, morbidity, and consequently the cost of the disease is esophagojejunal anastomotic leakage (EAL)<sup>4-6</sup>. EAL rates are reported between 2.1 and 14.7 % in literature<sup>4-6</sup>. In our study, we detected EAL in one patient (2.3 %), which was compatible with the literature. Most EAL is caused by technical errors not detected during surgery<sup>22,23</sup>. With the widespread use of staplers, the rates of anastomotic leaks have decreased<sup>3,22,24</sup>. Once an anastomotic leak is observed, the mortality rate increases<sup>4</sup>. Evaluation of doughnuts alone may not be sufficient after an EJ anastomosis. In this study, the integrity of the doughnuts was complete in both groups, but we detected abnormal findings with IOE in seven patients and fixed the problem intraoperatively. After the additional intervention, supporting sutures, or

endoscopic control, no postoperative anastomosis-related complications were observed in those patients.

IOE has been carried out for many years to evaluate tumor localization and anastomosis in colon surgery<sup>11-14</sup>. IOE is frequently used in bariatric surgery to evaluate gastric conduit and anastomosis<sup>15,16</sup>. There are limited studies about the control of anastomosis with IOE in gastric cancer surgery<sup>17-19</sup>. Studies evaluating the anastomosis after gastric cancer surgery in the literature are air insufflation with a nasogastric tube, methylene blue leak test, or endoscopic assessment<sup>9,10,17-19</sup>. In three of these studies, anastomosis was evaluated in detail by endoscopy. Evaluation by endoscopy reduces the complication rates associated with anastomosis<sup>19</sup>. Our study did not observe an anastomotic leak in the IOE group.

After EAL develops, treatment can be carried out by different methods. Regardless of the technique used for treatment, the length of hospital stay and the number of re-operations will increase, and it will be necessary to struggle with life-threatening complications<sup>23,25,26</sup>. There was a patient with an anastomotic leak in the non-IOE group. The hospitalization period of this patient was 152 days, and he was operated on six times during this period. IOE may help to prevent such complications by detailed evaluation of anastomosis and intervention. No complication related to the endoscopic procedure was seen in the previous studies<sup>13,15,17-19</sup>. Similarly, there was no complication related to endoscopy in the current study.

It is known that prolonged operation time adversely affects post-op complications<sup>6</sup>. The average endoscopic intervention time was 16 minutes in patients who had an abnormal finding related to the anastomosis. The mean procedure time was eight minutes in patients of the IOE group with no intervention. There was no significant difference between the total operation times in both groups (Table 1).

We were not performing routine endoscopies before July 2019. After this time, we are currently routinely performing endoscopy after EJ anastomosis. Our study's limitation is the lack of randomization. Postoperative complications are one of the main reasons for the high cost of cancer surgery<sup>8</sup>. IOE may help to decrease anastomosis-related complication rates and thus cost. Another limitation is that cost calculation was not made in our study.

**Table 3:** The clinical courses of intervened patients during intraoperative endoscopy.

Abnormal findings during intraoperative endoscopy	Number	Performed procedures	Patient's results
Mucosal bleeding	4	3 Endoscopic bleeding control 1 Supporting suture	Discharge as hassle-free
Air leak	2	Supporting suture	Discharge as hassle-free
Mucosal detachment	1	Supporting suture	Discharge as hassle-free

The comorbidities and patient's nutritional status should be determined preoperatively, and necessary precautions should be taken. Improving perioperative patient care can reduce complications associated with anastomosis by accelerating wound healing<sup>27-30</sup>.

In conclusion, IOE is a safe method for evaluating EJ anastomosis after total gastrectomy. It can reduce complications associated with anastomosis. However, we couldn't observe a significant difference in our study. The small number of enrolled patients and single-center retrospective nature are the main limitations of the current study. Multi-centered prospective randomized controlled trials with a large number of patients are required to evaluate the effectiveness of IOE.

### Conflicts of Interest

The authors declare no conflicts of interest.

### References

- Bray F, Ferlay J, Soerjomataram I, Siegel RL, Torre LA, Jemal A. Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. *CA Cancer J Clin.* 2018; 68: 394-424.
- Japanese Gastric Cancer Association. Japanese gastric cancer treatment guidelines 2018 (5th edition). *Gastric Cancer.* 2021; 24: 1-21.
- Gertsen EC, Goense L, Brenkman HJF, van Hillegersberg R, Ruurda JP. Identification of the clinically most relevant postoperative complications after gastrectomy: a population-based cohort study. *Gastric Cancer.* 2020; 23: 339-348.
- Selby LV, Vertosick EA, Sjoberg DD, Schattner MA, Janjigian YY, Brennan MF, et al. Morbidity after Total Gastrectomy: Analysis of 238 patients. *J Am Coll Surg.* 2015; 220: 863-871.e2.
- Li SS, Costantino CL, Mullen JT. Morbidity and Mortality of Total Gastrectomy: a Comprehensive Analysis of 90-Day Outcomes. *J Gastrointest Surg.* 2019; 23: 1340-1348.
- Deguchi Y, Fukagawa T, Morita S, Ohashi M, Saka M, Katai H. Identification of risk factors for esophagojejunal anastomotic leakage after gastric surgery. *World J Surg.* 2012; 36: 1617-1622.
- Wang S, Xu L, Wang Q, Li J, Bai B, Li Z, et al. Postoperative complications and prognosis after radical gastrectomy for gastric cancer: a systematic review and meta-analysis of observational studies. *World J Surg Oncol.* 2019; 17: 52.
- Goense L, van Dijk WA, Govaert JA, van Rossum PS, Ruurda JP, van Hillegersberg R. Hospital costs of complications after esophagectomy for cancer. *Eur J Surg Oncol.* 2017; 43: 696-702.
- Celik S, Almali N, Aras A, Yilmaz Ö, Kızıltan R. Intraoperatively Testing the Anastomotic Integrity of Esophagojejunostomy Using Methylene Blue. *Scand J Surg.* 2017; 106: 62-67.
- Kanaji S, Ohyama M, Yasuda T, Sendo H, Suzuki S, Kawasaki K, et al. Can the intraoperative leak test prevent postoperative leakage of esophagojejunal anastomosis after total gastrectomy? *Surg Today.* 2016; 46: 815-820.
- Lanthaler M, Biebl M, Mittermair R, Ofner D, Nehoda H. Intraoperative colonoscopy for anastomosis assessment in laparoscopically assisted left-sided colon resection: is it worthwhile? *J Laparoendosc Adv Surg Tech A.* 2008; 18: 27-31.
- Li VK, Wexner SD, Pulido N, Wang H, Jin HY, Weiss EG, et al. Use of routine intraoperative endoscopy in elective laparoscopic colorectal surgery: can it further avoid anastomotic failure? *Surg Endosc.* 2009; 23: 2459-2465.
- Kawai K, Iida Y, Ishihara S, Yamaguchi H, Nozawa H, Hata K, et al. Intraoperative colonoscopy in patients with colorectal cancer: Review of recent developments. *Dig Endosc.* 2016; 28: 633-640.
- Vallicelli C, Pirrera B, Alagna V, Fantini E, Palini GM, Zanini N, et al. Intraoperative endoscopy with immediate suture reinforcement of the defect in colorectal anastomosis: a pilot study. *Updates Surg.* 2020; 72: 999-1004.
- Minhem MA, Safadi BY, Tamim H, Mailhac A, Alami RS. Does intraoperative endoscopy decrease complications after bariatric surgery? Analysis of American College of Surgeons National Surgical Quality Improvement Program database. *Surg Endosc.* 2019; 33: 3629-3634.
- Haddad A, Tapazoglou N, Singh K, Averbach A. Role of intraoperative esophagogastroenteroscopy in minimizing gastrojejunostomy-related morbidity: experience with 2,311 laparoscopic gastric bypasses with linear stapler anastomosis. *Obes Surg.* 2012; 22: 1928-1933.
- Lieto E, Orditura M, Castellano P, Pinto M, Zamboli A, De Vita F, et al. Endoscopic intraoperative anastomotic testing may avoid early gastrointestinal anastomotic complications. A prospective study. *J Gastrointest Surg.* 2011; 15: 145-152.
- Nishikawa K, Yanaga K, Kashiwagi H, Hanyuu N, Iwabuchi S. Significance of intraoperative endoscopy in total gastrectomy for gastric cancer. *Surg Endosc.* 2010; 24: 2633-2636.
- Park JH, Jeong SH, Lee YJ, Kim TH, Kim JM, Kim DH, et al. Safety and efficacy of post-anastomotic intraoperative endoscopy to avoid early anastomotic complications during gastrectomy for gastric cancer. *Surg Endosc.* 2020; 34: 5312-5319.
- 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: 205-213.
- Amin MB, Edge SB, Greene FL, Byrd DR, Brookland RK, Washington MK, et al (eds). *AJCC Cancer Staging Manual.* Springer Nature, Switzerland, 2017.
- Migita K, Takayama T, Matsumoto S, Wakatsuki K, Enomoto K, Tanaka T, et al. Risk factors for esophagojejunal anastomotic leakage after elective gastrectomy for gastric cancer. *J Gastrointest Surg.* 2012; 16: 1659-1665.
- Makuuchi R, Irino T, Tanizawa Y, Bando E, Kawamura T, Terashima M. Esophagojejunal anastomotic leakage following gastrectomy for gastric cancer. *Surg Today.* 2019; 49: 187-196.
- Inokuchi M, Otsuki S, Fujimori Y, Sato Y, Nakagawa M, Kojima K. Systematic review of anastomotic complications of esophagojejunostomy after laparoscopic total gastrectomy. *World J Gastroenterol.* 2015; 21: 9656-9665.
- Tanaka H, Tamura T, Toyokawa T, Muguruma K, Kubo N, Sakurai K, et al. C-reactive protein elevation ratio as an early predictor of postoperative severe complications after laparoscopic gastrectomy for gastric cancer: a retrospective study. *BMC Surg.* 2019; 19: 114.
- Kim YJ, Shin SK, Lee HJ, Chung HS, Lee YC, Park JC, et al. Endoscopic management of anastomotic leakage after gastrectomy for gastric cancer: how efficacious is it? *Scand J Gastroenterol.* 2013; 48: 111-118.
- Hsueh SW, Liu KH, Hung CY, Kuo YC, Tsai CY, Hsu JT, et al. Significance of the Glasgow Prognostic Score in Predicting the Postoperative Outcome of Patients with Stage III Gastric Cancer. *J Clin Med.* 2019; 8: 1448.
- Kim SH, Son SY, Park YS, Ahn SH, Park DJ, Kim HH. Risk Factors for Anastomotic Leakage: A Retrospective Cohort Study in a Single Gastric Surgical Unit. *J Gastric Cancer.* 2015; 15: 167-175.
- Kanda M. Preoperative predictors of postoperative complications after gastric cancer resection. *Surg Today.* 2020; 50: 3-11.
- Schietroma M, Cecilia EM, Carlei F, Sista F, De Santis G, Piccione F, et al. Prevention of anastomotic leakage after total gastrectomy with perioperative supplemental oxygen administration: a prospective randomized, double-blind, controlled, single-center trial. *Ann Surg Oncol.* 2013; 20: 1584-1590.