Original Article

Anastomotic complications after laparoscopic total gastrectomy with esophagojejunostomy constructed by circular stapler (OrVil™) versus linear stapler (overlap method)

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Short running head: Comparative study of esophagojejunostomy

Abstract

Background

Esophagojejunostomy after laparoscopic total gastrectomy (LTG) is the most technically difficult type of anastomosis; thus, anastomotic complications such as leakage and stenosis sometimes occur. Identification of the safest anastomotic procedure is important for successful LTG. We have performed LTG since 2004 either with a circular stapler using an OrVil™ anvil or via the overlap Orringer method with a linear stapler. This retrospective study aimed to determine which method results in a lower incidence of anastomotic complications in patients undergoing LTG.

Methods

Data on 188 consecutive patients who underwent LTG between April 2004 and August 2016 were retrospectively reviewed. Patients were divided into those who underwent esophagojejunostomy performed via a circular stapler using an OrVil™ anvil (group C, n = 49) or via the overlap method (group L, n = 139).

Results

Anastomotic complications occurred in five of 188 esophagojejunostomies (2.7%). They comprised three cases of leakage (1.6%), and two of stenosis (1.1%). There was no significant difference in patient characteristics or hematological variables between groups C and L. There

was no significant difference between groups in operation time, blood loss, lymph node dissection, and intraoperative anastomotic problems. The rate of anastomotic complications was significantly lower in group L (0.7%, 1/139) than in group C (8.2%, 4/49; p = 0.005). In particular, anastomotic leakage in group L tended to be lower (0.7% 1/139) than in group C (4.1% 2/49); although this difference was not significant. The rate of anastomotic stenosis in group L was significantly lower (0%, 0/139) than in group C (4.1%, 2/49; p = 0.017). Furthermore multivariate analysis showed anastomotic procedure was an independent factor for anastomotic complication.

Conclusions

There were fewer anastomotic complications after overlap esophagojejunostomy than after esophagojejunostomy via the OrVil™ procedure, especially regarding anastomotic stenosis. We therefore recommend the overlap technique when performing esophagojejunostomy.

Keywords: Laparoscopic gastrectomy, Total gastrectomy, Gastric cancer, Esophagojejunostomy, Anastomotic complication

Introduction

Esophagojejunostomy after laparoscopic total gastrectomy (LTG) is the most technically difficult type of anastomosis in the field of laparoscopic gastrectomies; thus, anastomotic complications such as leakage and stenosis sometimes occur. Leakage from an esophagojejunostomy is a serious complication that requires long-term fasting and is occasionally life-threatening [1-6]. Anastomotic stenosis can be classified as edematous, membranous, or cicatricial. Edematous anastomoses usually require fasting for several weeks, whereas membranous and cicatricial stenoses require balloon dilation or, occasionally, revision surgery [5,7,8]. Therefore, identification of the safest anastomotic procedure is important for the success of LTG.

In the past, esophagojejunostomy was generally performed using a circular stapler. However, both anvil insertion and purse-string suturing were more difficult under laparoscopic conditions than in open surgery, and prevented LTG from being performed. These problems were resolved by the release of the OrVil™ transorally inserted anvil (Covidien Japan, Tokyo, Japan). In addition, the efficacy of using linear staplers to construct esophagojejunostomies has increasingly been recognized in the field of laparoscopic surgery [9,10]. During LTG in our institutes, we have performed esophagojejunostomy either via overlap anastomosis using a linear stapler according to the Orringer method or by a circular stapler using an OrVil™ anvil

since 2004 [11,12].

The aim of this retrospective study was to determine which of these two methods is superior in terms of reducing the incidence of anastomotic complications in patients undergoing LTG.

Materials and Methods

We started LTG since April 2004, and in this study, we retrospectively reviewed data from 188 consecutive patients who had undergone LTG between April 2004 and August 2016 in our hospitals. Anastomotic techniques changed during this period: from April 2004 to March 2011 we used either the OrVil™ or overlap techniques; from April 2011 to August 2016, all anastomoses were constructed by overlap esophagojejunostomy according to surgeon's preference (a philosophy that laparoscopic suturing skill level should be raised by usual surgery). Overall, esophagojejunostomies were constructed with circular staplers by the OrVil™ system in 49 patients (group C), and by the overlap method in 139 (group L). Patients' characteristics, hematological variables, operative factors and anastomotic complications were compared between group C and group L. All patients underwent gastrografin meal examination on postoperative day 3, and additionally when patients had abnormal temperatures, white blood cell counts, C-reactive protein concentrations, or suspected anastomotic stenosis. Anastomotic

leakage was considered present when confirmed by gastrografin examination. Cases of anastomotic stenoses were defined as those requiring balloon dilation or revision surgery.

This retrospective study was approved by the institutional review board of Hokkaido University Graduate School of Medicine. All procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Helsinki Declaration of 1964 and later versions. Informed consent was obtained from all patients for being included in the study. Gastric cancer was diagnosed in accordance with the Japanese Gastric Cancer Treatment Guidelines (2010) of the Japanese Gastric Cancer Association and Japanese classification of gastric carcinoma: 3rd English edition [13,14]

Anastomotic procedures

Circular stapler esophagojejunostomy constructed using the OrVil™ (group C): the esophagus was cut with a linear stapler for total gastrectomy, and a small hole was made in the center of the staple line for passing a connecting tube of the OrVil™ transorally inserted anvil (**Figure 1a, 1b**). A 25-mm diameter circular stapler was used in all cases. A circular stapler was docked with an anvil laparoscopically, and anastomosis was accomplished using the double-stapling technique (**Figure 1c**). The stump of the jejunum that was used for inserting the

circular stapler was closed with a linear stapler (**Figure 1d**). All anastomoses were performed air leak test and confirmed negative air leak.

Overlap esophagojejunostomy (group L): the esophagus was cut with a linear stapler for total gastrectomy, and an entry hole was created in the center or left half of the staple line for inserting the anvil of a linear stapler (**Figure 1a**). The jejunum was pulled up via the retro-colic route, and an incision was made 5 cm from the end of the jejunal stump; the cartridge of the linear stapler was inserted through this incision. A side-to-side esophagojejunostomy was constructed with a 45-mm long linear stapler, making the overlap as long as possible (**Figure 1b**). The entry hole was closed in two layers: a full-thickness running suture and interrupted seromuscular suture according to the original Orringer method [11] (**Figure 1c, 1d**). All anastomoses were performed air leak test and confirmed negative air leak.

Statistical analysis

IBM SPSS 22 statistical software for Windows (IBM, Armonk, New York, USA) was used for statistical analyses via the Student's *t*-test, Pearson's χ^2 test and logistic regression analysis. Differences with a p value of < 0.05 were considered statistically significant.

Results

Rate of anastomotic complications

Anastomotic complications occurred in five of 188 esophagojejunostomies (2.7%). They comprised three cases of leakage (1.6%), and two of stenosis (1.1%; Table 1). All anastomotic stenosis were appeared within two weeks after surgery.

Patient characteristics

There was no significant difference in patient characteristics or hematological variables including nutritional variables (total protein, serum albumin and lymphocyte count which sometimes used as a nutrition index [15,16]) between group C and group L. Pathological stage had not significant difference between two groups (Table 2).

Operative results

There was no significant difference between the two groups in operation time, blood loss, degree of lymph node dissection, and intraoperative anastomotic difficulty (Table 3). There was one case of intraoperative anastomotic difficulty in each group: the case in group C involved pinching of the mucosa of the efferent limb by the circular stapler, which required re-anastomosis; the case in group L was a jejunal stump injury caused by the edge of the linear stapler, which required re-anastomosis. Both cases occurred in the early phase of starting the LTG. The rate of anastomotic complications was significantly lower in group L (0.7%, 1/139) than in group C (8.2%, 4/49; $p = 0.005$). In particular, anastomotic leakage in group L (0.7%

1/139) tended to be lower than in group C (4.1% 2/49); however, this difference was not significant. The rate of anastomotic stenosis in group L (0%, 0/139) was significantly lower than in group C (4.1%, 2/49; p = 0.017; Table 3).

Risk factors of anastomotic complications

In univariate analysis for risk factor of anastomotic complication, preoperative hemoglobin (p=0.025), total protein (p=0.013) and serum albumin (p=0.015) were significantly lower in anastomotic complication + group. And Group L was significantly (p=0.005) lower incidence of anastomotic complications (Table 4). However, in multivariate analysis, significant difference was obtained in only anastomotic procedure (p=0.025) (Table 5).

Discussion

In recent years, esophagojejunostomies have usually been constructed using suturing devices; a technique that is safer and easier to perform than hand-sewing anastomoses [17]. However, anastomotic complications of esophagojejunostomy do occur, even when a suturing device has been used [1-8]. LTG requires a more sophisticated esophagojejunostomy technique than open total gastrectomy, and so the risk of anastomotic complications may increase. Thus, identifying the safest anastomotic procedure is important in minimizing anastomotic complications of esophagojejunostomy, especially in LTG.

Of the two major anastomotic complications examined in the present study, we consider anastomotic leakage to be the most important clinically. The rate of anastomotic leakage after esophagojejunostomy in LTG is reportedly 3.0%–6.5% [1, 4-6], and was 1.6% in the present study. In open surgery, the rate of anastomotic leakage is reportedly slightly lower at 2.1%–5.7% [1-3,5]. Some studies have reported patient-related factors such as age or pulmonary insufficiency as causes of anastomotic leakage [2,3]; however, most reports have concluded that anastomotic leakage is caused by technical errors [1-3,17]. Although patient-related factors associated with leakage are unavoidable, there are techniques that may reduce the risk of leakage. One technique used to reduce the risk of anastomotic leakage is the air leak test; however, 4.9% of patients with negative air leak tests reportedly have anastomotic leakage postoperatively [3]. Thus, the air leak test may only slightly reduce the incidence of anastomotic leakage. Also in this study, all anastomoses were performed air leak test with negative air leak, however, anastomotic leakage was happened.

Technical errors in esophagojejunostomy are partly attributable to the deep and dorsal location of the anastomotic site, hindering manipulation and visibility, and to the tension between the esophagus and jejunum. As almost all reported esophagojejunostomies have been constructed with circular staplers, most studies on anastomotic leakage of esophagojejunostomy have comprised only cases in which this type of stapler was used. Technical errors resulting in

anastomotic leakage are classified into two categories: errors in purse-string suturing (destruction of the muscular layer of the esophagus and inadequate purse-string sutures), and errors in using the circular stapler (using a circular stapler with an inappropriate diameter, rough insertion, and careless extraction of the stapler) [18]. The OrVil™ procedure can certainly reduce the purse-string suturing errors, but not the errors associated with the use of the circular stapler.

Recently, it has been reported that side-to-side esophagojejunostomy using a linear stapler (such as the overlap method) is associated with a smaller risk of anastomotic leakage, especially in the field of laparoscopic surgery [9,10]. Overlap side-to-side anastomosis, first reported by Orringer et al., was originally a cervical esophagogastric anastomosis designed to eliminate anastomotic leakage after esophageal cancer surgery [11]. The original procedure involved construction of a side-to-side cervical esophagogastric anastomosis with a linear stapler, with the entry incision for inserting the linear stapler then closed in two layers (full-thickness running suture as an inner layer and outer interrupted seromuscular suture). This procedure was expected to eliminate anastomotic leakage, as triple-layered stapling is more water-tight than a single- or double-stapled anastomosis; moreover, leakage from hand-sewn closure of the site of entry is uncommon [11]. However, we consider that an important additional reason that this procedure reduces the risk of leakage is that it is free of the technical

errors described above. In the present study, expected risk factors influencing on anastomotic leakage (patient's background, nutritional status, operation time and blood loss) had no significant difference between group C and group L, however, the rate of leakage in group L was lower than in group C. The OrVil™ procedure seems to be as safe as open surgery; however, the overlap procedure may be safer in terms of reducing anastomotic leakage.

The other anastomotic complication found in the present study was anastomotic stenosis. The rate of anastomotic stenosis after esophagojejunostomy in LTG is reportedly 3.2%–17% [5,8,12]; while in open surgery, the reported rate of anastomotic stenosis is slightly lower at 1.0%–4.1% [5,7,8]. The cause of anastomotic stenosis is often unknown; however, some authors have reported that risk factors for this complication include using 21-mm diameter circular staplers, female patients, double-staple technique anastomosis, and long-term postoperative fasting [7,8,18]. In the present study, the rate of anastomotic stenosis in group C was approximately the same as that reported in open total gastrectomy, which was significantly higher than in group L. We used a 25-mm diameter circular stapler for all group C patients; however, the OrVil™ procedure was applied via the double-staple technique. Furthermore, it is harder to feel the degree of traction when pulling the stump of the esophagus to dock an anvil and circular stapler in laparoscopic surgery than in open surgery; this can be problematic if too much tension is inadvertently applied, as strong traction is a risk factor for stenosis. In the

present study, no patients who underwent overlap esophagojejunostomy developed anastomotic stenosis. One possible explanation for this difference is the wide anastomotic stoma, which comprises a side-to-side stapled suture and hand-sewn closure of the entry hole. Additionally, whole circumference inverting stapler anastomosis tends to result in membranous stenosis; however, overlap anastomosis is not a circumferential inverted stapler anastomosis because it has a hand-sewn part.

Finally, on the standpoint of risk factors for anastomotic complications, we examined by both univariate and multivariate analysis between anastomotic complication – group and anastomotic complication + group. In patient's backgrounds and operative factors, hemoglobin, total protein, serum albumin and operative procedure (OrVil™ procedure vs. overlap technique) were detected as risk factors. This result was expectable because anemia and poor nutritional status were commonly regarded as risk factors for postoperative complications. Next in the examination of multivariate analysis, hemoglobin, total protein, serum albumin and operative procedure were selected for variables. The result showed that a significant difference was found for operative procedure only. Esophagojejunostomy using overlap technique has possibility for reducing anastomotic complication even in high risk patient.

Our findings indicate that overlap anastomosis is better at preventing anastomotic complications than anastomosis using the OrVil™ system. However, the disadvantage of

overlap anastomosis is that it requires a sophisticated suturing technique. In group L, one case of leakage occurred after a surgery that was performed by a surgeon with no LTG experience. Additionally, although in some institutions the entry incision is closed with a single layer full-thickness suture, we perform two layer suturing as described in the original Orringer's method, which entails a risk of prolonging the operation time [9,10]. To make this suturing easier and minimize prolongation of the operation time, we create a full-thickness suture with a running suture using a V-Loc™ wound closure device (Covidien Japan, Tokyo, Japan) and an outer seromuscular interrupted suture created by extracorporeal knot-tying. This technique enables us to construct an anastomosis within 30 minutes.

In conclusion, overlap esophagojejunostomy achieved a lower incidence of anastomotic complications than the OrVil™ procedure, especially in anastomotic stenosis. Although the OrVil™ procedure seems to be technically easier, we recommend the overlap technique when performing esophagojejunostomies in LTG because of the reduced incidence of anastomotic complications.

Author Disclosures

Dr. Hideki Kawamura, Dr. Yosuke Ohno, Dr. Nobuki Ichikawa, Dr. Tadashi Yoshida, Dr. Shigenori Homma, Dr. Masahiro Takahashi, and Dr. Akinobu Taketomi have no conflicts of

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Figure legends

Figure 1. Circular stapler esophagojejunostomy constructed using the OrVil™ system

a. A connecting tube of the OrVil™ transorally inserted circular stapler anvil was passed thorough the center of the staple line.

b. An OrVil™ anvil was set for anastomosis using the double-stapling technique.

c. A circular stapler was docked with an anvil laparoscopically.

d. The stump of the jejunum that had been used for inserting the circular stapler was closed using a linear stapler.

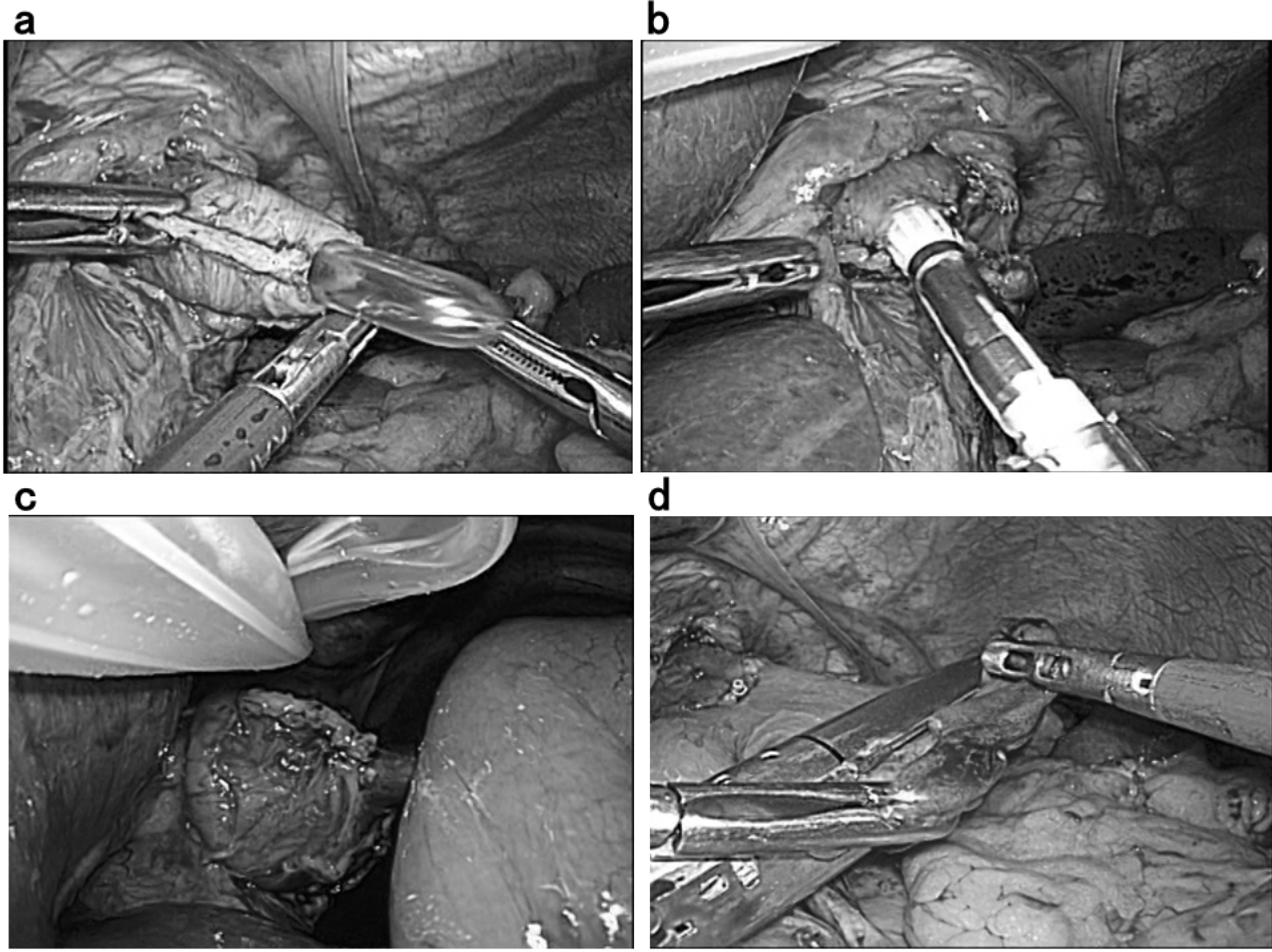
Figure 2. Overlap esophagojejunostomy using a linear stapler

a. The center or left half of the staple line was cut to create the entry incision for inserting the anvil of the linear stapler.

b. A side-to-side esophagojejunostomy was constructed with a 45-mm long linear stapler.

c. The inner layer of the entry incision was closed with a full-thickness running suture using a V-Loc wound closure device.

d. The outer layer of the entry incision was closed with an interrupted seromuscular suture.


a
b
c
d

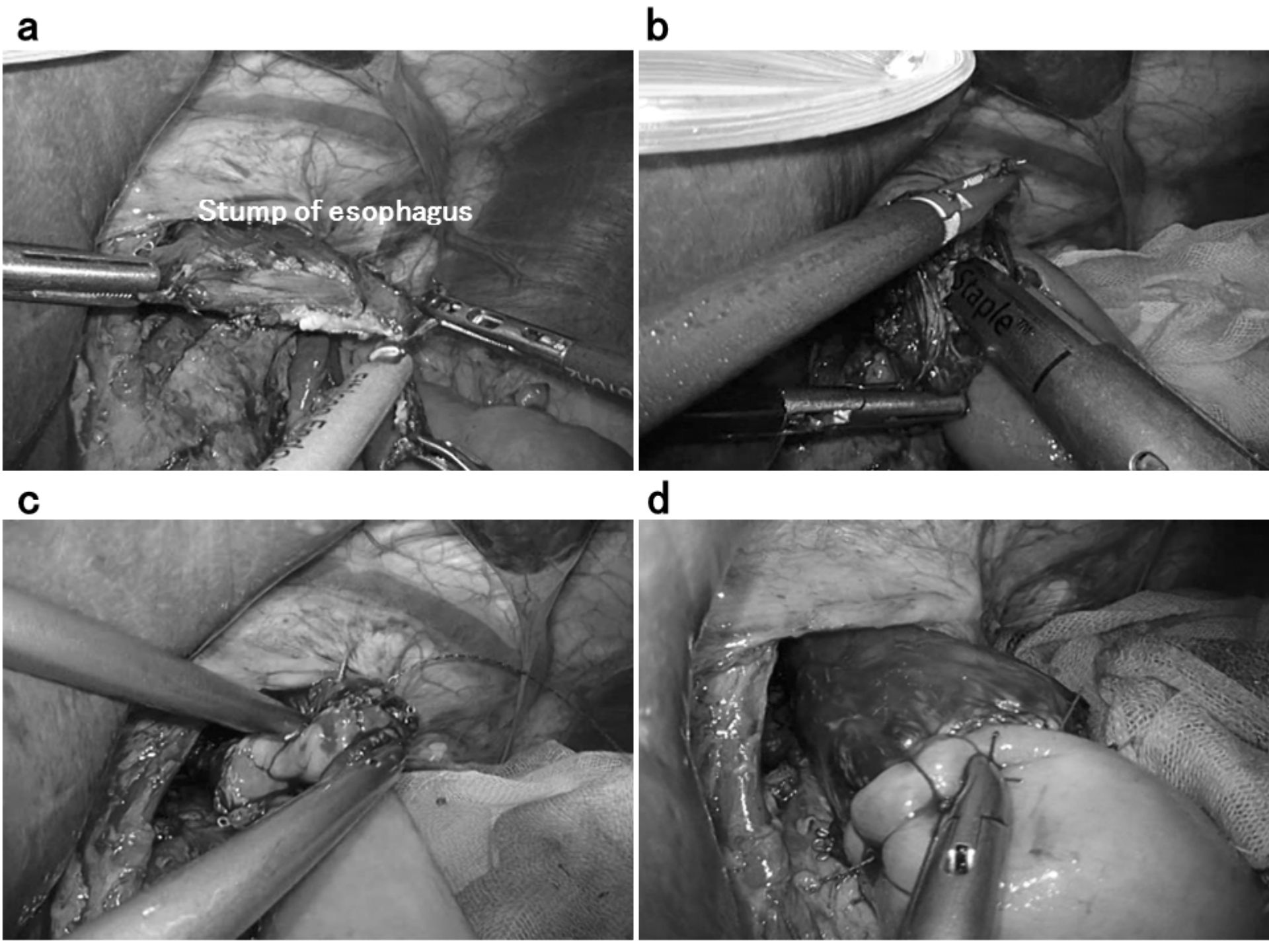

a
Stump of esophagus
b
Staple
c
d

Table 1 Anastomotic complications of esophagojejunostomy

		Esopagojejunostomy (n=188)
Anasomotic complications	-	183(97.3%)
	+	5(2.7%)
Details		
Anastomotic leakage	-	185(69.4%)
	+	3(1.6%)
Anastomotic stenosis	-	186(98.9%)
	+	2(1.1%)

Table 2 Patient's background compared between group C and group L

		Group C (n=49)	Group L (n=139)	P
Sex	Male	30(61.2%)	99(71.2%)	0.195
	Female	19(38.8%)	40(28.8%)	
Age		66.8±11.0	66.5±10.5	0.863
BMI		22.9±3.3	23.3±2.9	0.533
ASA	1	17(34.7%)	37(26.6%)	0.213
	2	23(46.9%)	87(62.6%)	
	3	9(18.4%)	15(10.8%)	
COPD	-	45(91.8%)	129(92.8%)	0.761
	+	4(8.2%)	10(7.2%)	
Chronic steroid usage	-	48(98.0%)	138(99.3%)	0.454
	+	1(2.0%)	1(0.7%)	
Neoadjyuvant chemotherapy	-	49(100%)	137(98.6%)	1.000
	+	0(0%)	2(1.4%)	
WBC (/μL)		5671±1372	5951±2004	0.367
Hemoglobin (g/dL)		12.7±2.2	12.8±1.8	0.750

Total protein (g/dL)		6.9±0.5	6.9±0.5	0.286
Serum albumin (g/dL)		4.1±0.54	4.0±0.4	0.079
Lymphocyte (/μL)		1691±702	1668±496	0.812
Pathological stage	1	40(81.6%)	113(81.3%)	0.700
	2	7(14.3%)	15(10.8%)	
	3	1(2.0%)	8(5.8%)	
	4	1(2.0%)	3(2.2%)	

BMI Body mass index; ASA American Society of Anesthesiology

COPD Chronic obstructive pulmonary disease

Table 3 Operative results compared between group C and group L

		Group C (n=49)	Group L (n=139)	P
Operation time (min)		259.5±51.4	276.5±53.0	0.053
Bleeding (mL)		53.3±70.0	69.7±116.6	0.355
Lymph node dissection	D1+	47(95.9%)	132(95.0%)	0.788
	D2	2(4.1%)	7(5.0%)	
Intraoperative anastomotic trouble	-	48(98.0%)	138(99.3%)	0.438
	+	1(2.0%)	1(0.7%)	
Anasomotic complications	-	45(91.8%)	138(99.3%)	0.005 *
	+	4(8.2%)	1(0.7%)	
Details				
Anastomotic leakage	-	47(95.9%)	138(99.3%)	0.106
	+	2(4.1%)	1(0.7%)	
Anastomotic stenosis	-	47(95.9%)	139(100%)	0.017 *
	+	2(4.1%)	0(0%)	

* $p<0.05$

Table 4 Comparison between anastomotic complication + group and – group

		Anastomotic complication - (n=183)	Anastomotic complication + (n=5)	P
Sex	Male	126(68.9%)	3(60%)	0.650
	Female	57(31.1%)	2(40%)	
Age		66.6±10.6	66.6±11.6	0.998
BMI		23.3±3.0	24.2±14.1	0.442
ASA	1	53(29.0)	1(20%)	0.750
	2	106(57.9%)	4(80%)	
	3	24(13.1%)	0(0%)	
COPD	-	169(92.3%)	5(100%)	1.000
	+	14(7.7%)	0(0%)	
Chronic steroid usage	-	181(98.9%)	5(100%)	1.000
	+	2(1.1%)	0(0%)	
Neoadjyuvant chemotherapy	-	181(98.9%)	5(100%)	1.000
	+	2(1.1%)	0(0%)	

WBC (/μL)		5903±1880	4980±130	0.275
Hemoglobin (g/dL)		12.9±1.8	11.0±2.8	0.025 *
Total protein (g/dL)		6.9±0.5	6.3±0.5	0.013 *
Serum albumin (g/dL)		4.1±0.4	3.6±0.3	0.015 *
Lymphocyte (/μL)		1684±557	1333±238	0.162
Lymph node dissection	D1+	175(95.6%)	4(80%)	0.220
	D2	8(4.4%)	1(20%)	
Operation time (min)		272.2±53.2	265.8±47.8	0.998
Bleeding (mL)		66.2±107.6	35.8±41.3	0.530
Anastomotic procedure	Group C	138(75.4%)	1(20%)	0.005 *
	Group L	45(24.6%)	4(80%)	
Intraoperative anastomotic trouble	-	181(98.9%)	5(100%)	1.000
	+	2(1.1%)	0(0%)	
Pathological stage	1	148(80.9%)	5(100%)	0.759
	2	22(12.0%)	0(0%)	
	3	9(4.9%)	0(0%)	
	4	4(2.2)	0(0%)	

BMI Body mass index; ASA American Society of Anesthesiology

COPD Chronic obstructive pulmonary disease

* $p<0.05$

Table 5 Multple logistic regression analysis between anastomotic complication + group and – group

	Hazard ratio	95% confidence interval	P
Hemoglobin (g/dL)	1.007	0.541-1.872	0.983
Total protein (g/dL)	0.258	0.029-2.322	0.227
Serum albumin (g/dL)	0.075	0.003-1.741	0.107
Anastomotic procedure	0.047	0.003-0.681	0.025 *

* $p<0.05$