World J Surg (2019) 43:1746–1755
https://doi.org/10.1007/s00268-019-04938-8

ORIGINAL SCIENTIFIC REPORT

The Impact of Circular Stapler Size on the Incidence of Cervical Anastomotic Stricture After Esophagectomy

Takahiro Hosoi[1,2] · Tetsuya Abe[1,2] · Norihisa Uemura[1,2] · Eiji Higaki[1,2] · Ryosuke Kawai[1,2] · Jiro Kawakami[1,2] · Byonggu An[1] · Masato Nagino[2] · Yasuhiro Shimizu[1,2]

Published online: 7 March 2019

Abstract

Background Cervical anastomotic stricture after esophagectomy is a serious complication that adversely affects postoperative recovery, nutritional status and quality of life. Cervical anastomosis by a circular stapler (CS) has been widely accepted as a simple and convenient method, but anastomotic strictures are likely to occur. The aim of this study was to investigate an association between CS size and the incidence of anastomotic stricture after cervical esophagogastric anastomosis performed by a CS.

Methods Between April 2011 and March 2016, 236 consecutive patients underwent cervical esophagogastric anastomosis by a CS via a retrosternal route after esophagectomy for esophageal cancer. These patients were divided into according to CS size for the procedure as follows: small-sized (25 mm) CS group (SG, n = 116) and large-sized (28 or 29 mm) CS group (LG, n = 120). The clinical data of patients were analyzed retrospectively to compare the two groups.

Results Overall, anastomotic strictures were observed in 90 patients (38%). The incidence of anastomotic stricture was significantly lower in the LG than the SG (23% vs. 53%, $p < 0.001$) (Table 3). Chronic obstructive pulmonary disease (COPD: FEV1.0% <70%) (OR 2.35, 95% CI = 1.09–5.14; $p = 0.029$), anastomotic leakage (OR 8.97, 95% CI = 2.69–41.30; $p < 0.001$), and a small-sized CS (OR 3.42, 95% CI = 1.82–6.62; $p < 0.001$) were independent risk factors for anastomotic stricture in the multivariate analysis.

Conclusions If possible, a large-sized CS should be used to prevent cervical anastomotic strictures when performing cervical anastomoses by CS.

Introduction

The techniques of esophagogastric anastomosis with a gastric conduit after esophagectomy raise great concerns about preventing anastomotic complications, such as leakage and stricture. However, the optimal anastomotic technique after esophagectomy has not yet been identified.

Cervical anastomosis by means of a circular stapler (CS) is widely accepted as a simple and convenient method that requires less operation time and allows a low incidence of anastomotic leakage. Nevertheless, the incidence of cervical anastomotic stricture reportedly ranges from 17 to 48% [1–5]. The technique using a CS has a higher

Electronic supplementary material The online version of this article (https://doi.org/10.1007/s00268-019-04938-8) contains supplementary material, which is available to authorized users.

✉ Takahiro Hosoi
tabe@aichi-cc.jp

[1] Department of Gastroenterological Surgery, Aichi Cancer Center Hospital, 1-1 Kanokoden, Chikusa-ku, Nagoya, Aichi 464-8681, Japan

[2] Division of Surgical Oncology, Department of Surgery, Nagoya University Graduate School of Medicine, Nagoya, Japan

incidence of anastomotic strictures than the hand-sewn technique [1, 2] Furthermore, cervical anastomoses are associated with an increased risk of anastomotic stricture compared with intrathoracic anastomoses [6–8].

Anastomotic stricture is a serious complication that adversely affects postoperative recovery, nutritional status and quality of life. Several studies reported that a small-sized CS contributed to the high incidence of anastomotic strictures after esophagectomy [1, 9–12]. However, other studies reported contradictory conclusions [13, 14]. Moreover, these studies included patients with cervical anastomoses as well as those with intrathoracic anastomoses. Few studies have tried to investigate an association between the CS size and the incidence of anastomotic stricture in patients with a cervical anastomosis only. Therefore, whether the CS size affects the incidence of cervical anastomotic stricture remains controversial.

The aim of this study was to investigate an association between CS size and the incidence of anastomotic stricture after cervical esophagogastric anastomosis performed by a CS.

Methods

Patients

Between April 2011 and March 2016, 328 consecutive patients underwent transthoracic esophagectomy with lymphadenectomy for thoracic esophageal cancer at the Aichi Cancer Center Hospital. Of these, 236 patients underwent a cervical esophagogastric anastomosis by a CS via the retrosternal route. The 92 patients who underwent other reconstructions (n = 46) or had other anastomotic techniques (n = 46) were excluded. For the analysis, patients were divided into a small-sized CS (25 mm) group (SG, n = 116) and a large-sized CS (28 or 29 mm) group (LG, n = 120). The clinical data of these 236 patients were analyzed retrospectively to compare the two groups (Fig. 1). The clinical staging of tumors was performed according to the 7th edition of the TNM classification [15]. The review board of the Aichi Cancer Center Hospital approved this study.

Surgical procedure

All patients with thoracic esophageal cancer underwent either transthoracic esophagectomy via right thoracotomy or prone thoracoscopic esophagectomy with lymphadenectomy. We introduced thoracoscopic esophagectomy in April 2012.

We adopted gastric reconstruction as the first choice of alimentary tract reconstruction after esophagectomy. In patients ineligible for gastric reconstruction because of postgastrectomy or concurrent gastric cancer, we performed colonic or jejunal reconstruction.

Using linear staplers, we created an approximately 4-cm gastric conduit that partially preserved the greater omentum. The gastric conduit was pulled-up to the neck via the retrosternal route. We performed a cervical esophagogastric anastomosis on the left side of the neck using a CS. The CS method consisted of an end-to-side anastomosis performed by a 25 mm or 29 mm CS (ILS®, Ethicon, Tokyo, Japan) and a 28 mm CS (EEA®, Covidien, Tokyo, Japan).

We routinely used a small-sized CS irrespective of the esophageal diameter between April 2011 and January 2014. However, the incidence of anastomotic stricture was comparatively high (51%) during this period. We hypothesized that the size of a CS affects the incidence of anastomotic stricture. In February 2014, we changed our strategy so that a large-sized CS (28- or 29-mm CS) was routinely used.

Our insertion method for the anvil is shown in Fig. 2. We measured the esophageal diameter with the esophagus extended laterally after intravenous injection of 10 mg of scopolamine butylbromide to relax the esophageal muscular layer. If the diameter was 30 mm or larger, we used a large-sized CS (Fig. 2a). We grasped the esophagus at two points and inserted the anvil sideways into the cervical esophagus (Fig. 2b). The body of the CS was inserted through the gastrostomy at the top of the gastric conduit, and the anastomosis was created at the greater wall of the gastric conduit. However, if the esophageal diameter is smaller than 30 mm, inserting the anvil safely is difficult. Therefore, we used a small-sized CS when the esophageal diameter was smaller than 30 mm to avoid damage to the esophageal walls upon insertion of the anvil. After completion of the anastomosis, the proximal end of the gastric conduit was excised at approximately 2 cm from the anastomosis using a linear stapler, and the gastric conduit was gently pulled down in the caudal direction to straighten the cervical esophagus and the gastric conduit.

Postoperative management

The basic policy of postoperative management was identical for the two groups. All patients were extubated in the operating room. They were admitted to the intensive care unit for systemic monitoring. Until April 2015, a contrast swallow test was performed to diagnose anastomotic leakages on postoperative day (POD) 8. Recent studies have shown that computed tomography (CT) has higher sensitivity than a contrast swallow test for the diagnosis of anastomotic leakages [16, 17]. Therefore, starting in May 2015, we changed the diagnostic method from the contrast swallow test to CT, which was performed on POD 5 or 6

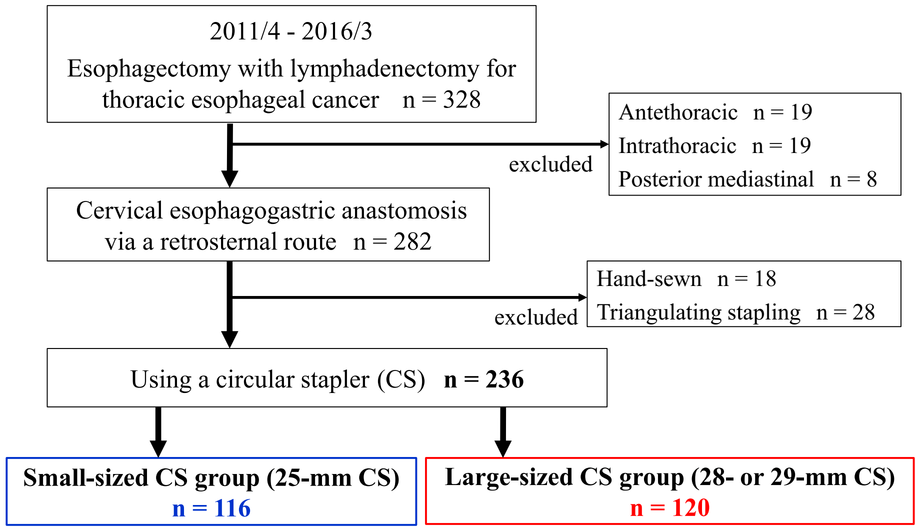

Fig. 1 The Consolidated Standards of Reporting Trials (CONSORT) flow diagram of patients

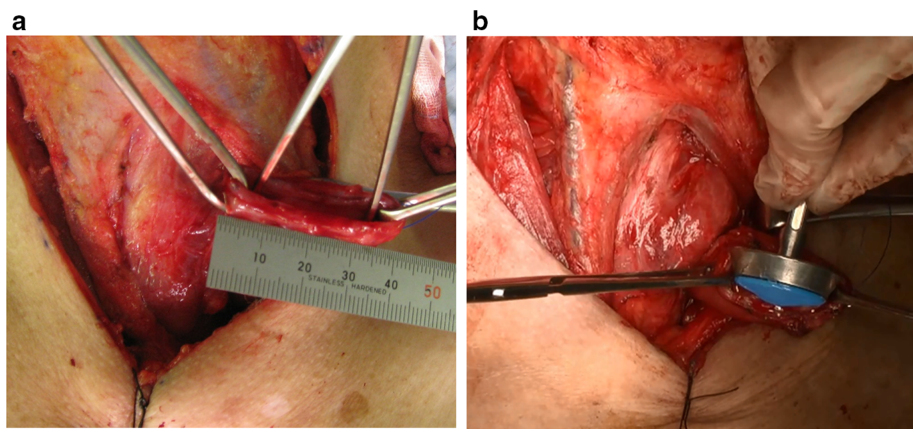

Fig. 2 Insertion method of anvil. **a** We measured the esophageal diameter with the esophagus extended laterally before the anvil insertion. **b** We grasped the esophagus at two points and inserted the anvil into the cervical esophagus sideways, like fastening a button

from May 2015. After these examinations, patients were allowed oral intake. With regard to postoperative analgesia, the patients were routinely prescribed postoperative non-steroidal anti-inflammatory drugs (NSAIDs) between POD 2 and 9 in addition to epidural anesthesia. However, we introduced postoperative acetaminophen as a substitute for NSAIDs in October 2015 because of concerns about the impairment of anastomotic healing by NSAIDs. After discharge, patients were examined at an outpatient visit monthly for 3 months. Thereafter, patients were examined every 3 months for 5 years after surgery. Upper gastrointestinal endoscopy was performed routinely at 12 months after surgery or whenever dysphagia developed. The median follow-up period was 1440 (range 131–2652) days.

Definition of postoperative complications

We defined anastomotic stricture as dysphagia requiring endoscopic balloon dilation or esophageal bougie with a Maloney dilator without evidence of locoregional recurrence of cancer. Anastomotic leakage was diagnosed by the presence of extraluminal contrast on a contrast swallow test, the presence of perianastomotic air bubbles or fluid collection outside the gastrointestinal tract on CT images, or the leakage of saliva through the cervical wound. Other postoperative complications were defined as greater than grade II according to the Clavien-Dindo classification [15].

Statistical analysis

Statistical analysis was performed using JMP® version 12 software (SAS Institute Inc., Cary, NC, USA). Differences in distribution frequencies between groups were evaluated by the Chi-square test or Fisher exact test for categorical variables and the Wilcoxon rank sum test for continuous variables. Univariate and multivariate logistic regression analyses were used to identify the risk factors for cervical anastomotic strictures. Univariate analyses were performed using the Chi-square test. Variables with a p value less than 0.1 according to univariate analysis were included for multivariate logistic regression analysis. A p value < 0.05 was considered to be statistically significant.

Results

Baseline characteristics

A total of 236 patients who underwent a cervical esophagogastric anastomosis by a CS via a retrosternal route were included in this study. The patients were divided into the SG ($n = 116$) and the LG ($n = 120$). We were able use a large-sized CS for 109 (93%) of the 117 patients undergoing esophagectomy during the time period when a large-sized CS was routinely used. However, we used a small-sized CS for 8 (7%) of those patients during this period, who had an esophageal diameter smaller than 30 mm (Supplementary Table 1).

The baseline characteristics of patients are summarized in Table 1. There were no significant between-group differences in age, gender, tumor location, comorbidities, clinical stage, or preoperative therapy. The rate of postoperative NSAIDs use was significantly higher in the SG than the LG (98% vs. 74%, $p < 0.001$).

To investigate the risk factors for a patient to have a small esophageal diameter (< 30 mm), we divided the 117 patients undergoing esophagectomy during the time period when a large-sized CS was routinely used into $a \geq$ 30-mm-esophageal-diameter group ($n = 109$) and $a <$ 30-mm group ($n = 8$), and compared the baseline characteristics between the two subgroups (Table 2). Female gender (62.5% vs. 18.4%, $p = 0.003$), shorter body height (1.52 m [range 1.44–1.72] vs. 1.66 m [range 1.45–1.82]; $p = 0.007$), and low body weight (47.6 kg [range 35.8–64.5] vs. median, 59.9 kg [range 34.4–82.5]; $p = 0.016$) were significant risk factors for small esophageal diameter (< 30 mm group) by the univariate analysis.

Surgical outcomes and postoperative complications

The surgical outcomes are summarized in Table 3. Thoracoscopic surgery was performed more frequently in the LG than the SG (53% vs. 29%, $p < 0.001$). The difference in surgical approach led to a longer operation time in the LG than the SG. Other outcomes were similar between the two groups.

The postoperative complications are summarized in Table 4. Overall, anastomotic strictures were observed in 90 patients (38%). The incidence of anastomotic stricture was significantly lower in the LG than in the SG (23% vs. 53%, $p < 0.001$). There were no significant between-group differences regarding the duration from the esophagectomy until the diagnosis of stricture (SG, 57 days vs. LG, 62 days), the duration of treatment for stricture (SG, 99 days vs. LG, 124 days) and the number of dilatations (SG, 4.5 times vs. LG, 5 times). CS size did not affect the course of treatment for patients with anastomotic strictures.

Overall, anastomotic leakage was observed in 19 patients (8%), with no significant difference between the two groups (SG, 10% vs. LG, 6%; $p = 0.203$). The incidence of other complications was not significantly different between the two groups.

Table 1 Baseline characteristics of patients

Variable	Small-sized CS group ($n = 116$)	Large-sized CS group ($n = 120$)	p
Age, median [range]	64 [44–86]	66 [40–81]	0.236
Gender, *n* male/female	95/21	98/22	0.964
BMI (kg/m^2), median [range]	21.8 [15.1–29.1]	21.4 [15–28.8]	0.145
Comorbidities			
Diabetes mellitus, *n* (%)	7 (6%)	10 (8%)	0.495
Cardiovascular disease, *n* (%)	51 (45%)	44 (37%)	0.253
COPD (FEV1.0% <70%), *n* (%)	24 (21%)	16 (14%)	0.096
Tumor location, *n* Ut/Mt/Lt	13/65/38	7/58/55	0.073
cStage, *n* I/II/III/IV	14/34/63/5	16/31/60/13	0.280
Preoperative therapy, *n* (%)	95 (82%)	93 (78%)	0.526
Neoadjuvant chemotherapy	87	82	
Neoadjuvant chemoradiotherapy	2	8	
Definitive chemoradiation	6	3	
Postoperative NSAIDs use, *n* (%)	114 (98%)	89 (74%)	<0.001

BMI body mass index, *COPD* chronic obstructive pulmonary disease, *NSAIDs* non-steroidal anti-inflammatory drugs

Table 2 Comparison of baseline characteristics between *a* ≥30-mm-esophageal-diameter group and <30-mm group (*n* = 117)

Variable	≥30-mm group (*n* = 109)	<30-mm group (*n* = 8)	*p*
Age, median [range]	66 [44–81]	68 [49–78]	0.336
Gender, *n* (%) male/female	89 (81.6%)/20 (18.4%)	5 (62.5%)/3 (37.5%)	0.003
Body height (m), median [range]	1.66 [1.45–1.82]	1.52 [1.44–1.72]	0.007
Body weight (kg), median [range]	59.9 [34.4–82.5]	47.6 [35.8–64.5]	0.016
BMI (kg/m^2), median [range]	21.5 [15.0–28.8]	19.7 [17.4–24.8]	0.255
Comorbidities			
Diabetes mellitus, *n* (%)	10 (9.2%)	1 (12.5%)	0.756
Cardiovascular disease, *n* (%)	41 (37.6%)	5 (62.5%)	0.164
COPD (FEV1.0% <70%), *n* (%)	12 (11.0%)	0 (0%)	0.322

BMI body mass index, *COPD* chronic obstructive pulmonary disease

Table 3 Surgical outcomes

Variable	Small-sized CS group (*n* = 116)	Large-sized CS group (*n* = 120)	*p*
Surgical approach, *n* (%) Transthoracic/thoracoscopic	82 (71%)/34 (29%)	56 (47%)/64 (53%)	<0.001
Dissection field, *n* (%) 2F/3F	17 (15%)/99 (85%)	19 (16%)/101 (84%)	0.546
Operation time (min), median [range]	441 [292–705]	463 [299–679]	0.024
Intraoperative blood loss (ml), median [range]	245 [20–1200]	245 [20–2220]	0.261
Postoperative hospital stay (days), median [range]	23 [11–139]	22 [5–111]	0.930

Table 4 Postoperative complications

Variable	Small-sized CS group (*n* = 116)	Large-sized CS group (*n* = 120)	*p*
Anastomotic stricture, *n* (%)	62 (53%)	28 (23%)	<0.001
Duration from surgery until diagnosis (days), median [range]	57 [20–756]	62 [21–420]	0.592
Duration of treatment (days), median [range]	99 [1–1010]	124 [1–1015]	0.567
Number of dilations, median [range]	4.5 [1–20]	5 [1–27]	0.415
Anastomotic leakage, *n* (%)	12 (10%)	7 (6%)	0.203
Surgical site infection, *n* (%)	14 (12%)	218 (15%)	0.511
Recurrent nerve palsy, *n* (%)	6 (5%)	11 (9%)	0.909
Pneumonia, *n* (%)	26 (22%)	23 (19%)	0.539
Chylothorax, *n* (%)	11 (9%)	9 (8%)	0.585
Arrhythmia, *n* (%)	18 (16%)	20 (17%)	0.810
Any postoperative complication, *n* (%)	93 (80%)	81 (68%)	0.027
Mortality, *n* (%)	1 (1%)	1 (1%)	0.980

Risk factors for cervical anastomotic stricture

The results of univariate and multivariate analyses of risk factors for anastomotic strictures are summarized in Table 5. By the univariate analysis, body mass index (BMI) > 25, chronic obstructive pulmonary disease (COPD: FEV1.0% predicted <70%), a small-sized CS, intraoperative blood loss (> 250 mL), anastomotic leakage, and postoperative NSAIDs use were significant risk factors for anastomotic strictures. By the multivariate

Table 5 Risk factors for anastomotic stricture ($n = 236$)

Variable	Univariate analysis		Multivariate analysis	
	Odds ratio (95% CI)	*p*	Odds ratio (95% CI)	*p*
Age > 70 years	0.69 (0.43–1.10)	0.094	0.58 (0.26–1.22)	0.153
Female	0.51 (0.28–1.18)	0.127		
BMI > 25 (kg/m^2)	2.51 (1.06–5.91)	0.032	2.22 (0.87–5.82)	0.095
Diabetes mellitus	0.88 (0.31–2.46)	0.802		
Cardiovascular disease	0.98 (0.58–1.68)	0.950		
COPD (FEV1.0% <70%)	2.76 (1.39–5.49)	0.003	2.35 (1.09–5.14)	0.029
Small-sized CS	3.38 (2.16–6.60)	<0.001	3.42 (1.82–6.62)	<0.001
Intraoperative blood loss (>250 ml)	1.65 (0.98–2.82)	0.061	1.46 (0.80–2.68)	0.217
Postoperative NSAIDs use	2.57 (1.07–6.19)	0.031	1.10 (0.42–3.16)	0.847
Anastomotic leakage	10.30 (2.91–36.50)	<0.001	8.97 (2.69–41.30)	<0.001
Pneumonia	1.58 (0.84–2.99)	0.154		
Arrhythmia	1.39 (0.69–2.80)	0.360		

BMI body mass index, *COPD* chronic obstructive pulmonary disease, *NSAIDs* non-steroidal anti-inflammatory drugs

analysis, COPD (odds ratio [OR] 2.35, 95% confidence interval [CI] = 1.09–5.14; $p = 0.029$), anastomotic leakage (OR 8.97, 95% CI = 2.69–41.30; $p < 0.001$), and small-sized CS (OR 3.42, 95% CI = 1.82–6.62; $p < 0.001$) were independent risk factors for anastomotic strictures.

Risk factors for cervical anastomotic stricture in patients without anastomotic leakage

The results of univariate and multivariate analyses of risk factors for anastomotic strictures in patients without anastomotic leakage are summarized in Table 6. By the univariate analysis, BMI > 25, COPD, a small-sized CS, and postoperative NSAIDs use were significant risk factors for anastomotic strictures. By the multivariate analysis, BMI (OR 2.63, 95% CI = 1.00–7.18; $p = 0.049$), COPD (OR 2.47, 95% CI = 1.11–5.56; $p = 0.027$) and a small-sized CS (OR 3.25, 95% CI = 1.69–6.42; $p < 0.001$) were independent risk factors for anastomotic strictures.

The effects of postoperative NSAIDs on development of anastomotic stricture and leakage in LG

We divided the LG patients into a NSAIDs (+) group and (−) group and compared the two subgroups to assess the effects of postoperative NSAIDs on the development of anastomotic stricture and leakage (Table 7). The between-group differences regarding the incidence of anastomotic

Table 6 Risk factors for anastomotic stricture in patients without anastomotic leakage ($n = 217$)

Variable	Univariate analysis		Multivariate analysis	
	Odds ratio (95% CI)	*p*	Odds ratio (95% CI)	*p*
Age >70 years	0.56 (0.30–1.03)	0.051	0.51 (0.22–1.10)	0.087
Female	0.50 (0.22–1.16)	0.087	0.56 (0.22–1.28)	0.172
BMI >25 (kg/m^2)	3.17 (1.29–7.82)	0.009	2.63 (1.00–7.18)	0.049
Diabetes mellitus	0.69 (0.21–2.23)	0.529		
Cardiovascular disease	1.03 (0.58–1.82)	0.923		
COPD (FEV1.0% <70%)	2.74 (1.31–5.73)	0.006	2.47 (1.11–5.56)	0.027
Small-sized CS	3.77 (2.07–6.85)	<0.001	3.25 (1.69–6.42)	<0.001
Intraoperative blood loss (>250 ml)	1.41 (0.80–2.48)	0.230		
Postoperative NSAIDs use	2.52 (0.99–6.43)	0.047	1.24 (0.46–3.75)	0.683
Pneumonia	1.75 (0.89–3.42)	0.100		
Arrhythmia	1.01 (0.46–2.24)	0.972		

BMI body mass index, *COPD* chronic obstructive pulmonary disease, *NSAIDs* non-steroidal anti-inflammatory drugs

Table 7 The effects of postoperative NSAIDs on development of anastomotic stricture and leakage in LG (n = 120)

The use of postoperative NSAIDs	Anastomotic stricture, n (%)	Odds ratio (95% CI)	p
(+) n = 89	21 (24%)	1.06 (0.40–2.80)	0.908
(−) n = 31	31 (23%)	Reference	
The use of postoperative NSAIDs	**Anastomotic leakage, n (%)**	**Odds ratio (95% CI)**	p
(+) n = 89	6 (6.7%)	2.17 (0.25–18.76)	0.472
(−) n = 31	1 (3.2%)	Reference	

NSAIDs non-steroidal anti-inflammatory drugs

stricture were not significant, as follows: (NSAIDs [+], 24% vs. NSAIDs [−], 23%; p = 0.908) and leakage (NSAIDs [+], 6.7% vs. NSAIDs [−], 3.2%; p = 0.472).

Discussion

This study demonstrated that the incidence of cervical anastomotic stricture after esophagectomy was associated with the CS size. The multivariate analysis found that a small-sized CS was an independent risk factor for cervical anastomotic strictures. Several studies support our finding and have recommended the use of a large-sized CS to reduce the incidence of anastomotic stricture after esophagectomy [1, 9–12]. In our study, the incidence of cervical anastomotic stricture was comparatively high (51%) during the time period when a small-sized CS was routinely used. However, previous studies that used a small-sized CS (21 or 25 mm) also found similar rates of cervical anastomotic stricture (42–48%) [3, 5]. Therefore, based on the results of these studies, we changed our strategy on the selection of CS size to overcome the high incidence of anastomotic stricture. By contrast, Yendamuri et al. and Johansson et al. did not find an association between CS size and the incidence of anastomotic stricture after esophagectomy [13, 14]. Therefore, whether or not CS size affects the incidence of cervical anastomotic stricture remains unclear. Moreover, these studies included patients with cervical anastomoses as well as those with intrathoracic anastomoses. To the best of our knowledge, few studies have investigated the association between CS size and the incidence of anastomotic stricture in patients with cervical anastomosis only. Hence, we investigated the relationship between CS size and incidence of stricture in patients receiving cervical anastomoses only, and did not include patients receiving intrathoracic anastomoses.

Wong et al. also found that the use of an EEA® increases a risk of anastomotic stricture compared to the use of an ILS® [9]. In this study, EEA® 28 mm was used for 11 patients in LG. However, the use of EEA® was not a risk factor for anastomotic stricture (OR 0.71, 95% CI = 0.14–3.49; p = 0.671) (Supplementary Table 2).

It should be noted that we were able to use a large-sized CS in 109 of 117 (93%) patients undergoing esophagectomy during the time period when a large-sized CS was routinely used in this study. Consequently, we reduced the incidence of anastomotic stricture (23%) without increasing the incidence of anastomotic leakage. We consider that sufficient relaxation of the esophageal and gastric muscular layers by intravenous injection of scopolamine butylbromide before anastomosis was one of the reasons why anastomotic leakage did not increase. This preparation for anastomosis makes it possible to perform the anastomosis without tension, which prevents damage of the esophageal and gastric walls when inserting the anvil or placing the staples. On the other hand, we used a small-sized CS for 8 of the 117 (7%) patients, whose esophageal diameter was smaller than 30 mm, to avoid damage to the esophageal wall upon insertion of the anvil. Selecting the appropriate CS size is important for preventing the occurrence of anastomotic leakage.

However, this study revealed that a small-sized CS was an independent risk factor for anastomotic stricture. Therefore, patients with a small esophageal diameter had a high risk for anastomotic stricture. To investigate the risk factors for small esophageal diameter (<30 mm), we divided the 117 patients into *a* ≥ 30-mm-esophageal-diameter group (n = 109) and <30-mm group (n = 8), and compared the baseline characteristics between the two subgroups. Female gender, short body height, and low body weight were significant risk factors for small esophageal diameter (<30 mm) by univariate analysis (Table 2). According to these results, it is likely that slender, petite women tend to have small esophageal diameters.

The overall incidence of anastomotic stricture in this study (38%) was relatively high compared with that of previous studies [1–5] although we reduced the incidence of anastomotic stricture by changing to the use of a large-sized CS. We think that the use of NSAIDs postoperatively was one of the reasons for the high incidence of anastomotic strictures. Postoperative NSAIDs use was a significant risk factor for anastomotic strictures by the univariate analysis. Several studies reported that NSAIDs might impair anastomotic healing and increase the risk of anastomotic leakage in colorectal surgery [18–22]. Additionally, Fjederholt et al. [23] demonstrated an association between the postoperative use of postoperative NSAIDs and the risk of anastomotic leakage after surgery for gastroesophageal junction cancers. Various mechanisms were suggested to explain the relationship between NSAIDs and anastomotic healing, such as reducing collagen production and impairing angiogenesis via downregulation of prostaglandins through cyclooxygenase inhibition. These mechanisms involved in the healing process might affect the development of anastomotic stricture. Most patients (86%) were prescribed postoperative NSAIDs for postoperative analgesia in this study, which may be the reason for the high incidence of anastomotic strictures. However, few studies have shown that postoperative NSAIDs use is associated with development of anastomotic stricture. To assess the effect of postoperative NSAIDs on development of anastomotic stricture and leakage, we divided the LG patients into a NSAIDs (+) group and (−) group and compared the two subgroups. The between-group differences regarding the incidence of anastomotic stricture and leakage were not significant (Table 7).

Anastomotic leakage was an independent risk factor for anastomotic strictures in our study. Anastomotic leakage has been reported previously to be the most common risk factor for anastomotic stricture after esophagectomy [3, 5, 24–26]. Anastomotic leakage is associated with poor perfusion and poor oxygenation of the anastomosis, which are causative factors for anastomotic stricture. Furthermore, the local inflammatory reaction associated with the leakage directly affects the development of anastomotic stricture [3, 23], and anastomotic leakage is considered a risk factor for refractory anastomotic stricture [3, 8]. However, there were only 19 patients (8%) with anastomotic leakage in this study, and CS size was the most powerful risk factor in 217 patients without anastomotic leakage (Table 6). Therefore, we consider that the CS size is extremely important for preventing a cervical anastomotic stricture.

This study demonstrated that COPD was also an independent risk factor for anastomotic strictures in the multivariate analysis. Poor oxygenation in COPD is associated with conduit ischemia, which leads to an anastomotic stricture [7, 25, 27]. Cooper et al. [27] reported that a low preoperative partial pressure of arterial oxygen (PaO2) was associated with poor gastric tissue oxygenation after mobilization of the stomach. Hanyu et al. [7] also reported that PaO2 was a risk factor for anastomotic strictures after esophagectomy. Therefore, carefully monitoring and managing the patient's blood pressure and peripheral artery oxygen saturation to maintain sufficient perfusion and oxygenation of the anastomosis is very important for preventing anastomotic strictures.

For reducing the incidence of cervical anastomotic stricture after esophagectomy, alternative anastomotic techniques such as a side-to-side anastomosis and a triangulating stapling anastomosis have been explored for use instead of the CS. These anastomotic techniques using a linear stapler have been suggested to lower incidence of anastomotic strictures significantly, which is possibly due to the larger anastomotic lumen regardless of esophageal diameter [28–33]. However, Hayata et al. [4] performed a randomized controlled trial (RCT) and found that a cervical triangulating stapling anastomosis using a linear stapler did not decrease the incidence of anastomotic stricture after esophagectomy, compared with a cervical anastomosis using a CS. Therefore, the optimal anastomotic technique after esophagectomy for reducing the incidence of anastomotic stricture remains unclear. This study demonstrated that a small-sized CS was an independent risk factor for anastomotic strictures after esophagectomy, and a CS sized as large as possible should be used to prevent anastomotic stricture when performing a cervical esophagogastric anastomosis by a CS. However, we were unable to use a large-sized CS for those patients whose esophageal diameter was smaller than 30 mm and who were therefore at high risk for anastomotic stricture because of the use of a small-sized CS. Therefore, for those patients whose esophageal diameter are smaller than 30 mm, alternative anastomotic techniques such as a hand-sewn or linear-stapler anastomosis might be preferable in order to avoid anastomotic stricture.

This study has several limitations. First, it was a single-center retrospective study. Second, it had a limited sample size and a study design with an inherent risk of bias. Third, the rate of postoperative NSAIDs use was significantly higher in the SG than the LG since our strategy of postoperative analgesia changed during the study period. This difference might have affected the results. Other perioperative management procedures were identical for the two groups. Despite the study limitations, our findings are beneficial for reducing the incidence of anastomotic stricture.

In conclusion, CS size was the most important risk factor for anastomotic strictures in patients without anastomotic leakage. Moreover, the use of a large-sized CS did not lead to an increased rate of anastomotic leakage. Therefore, we should use a large-sized CS if possible to prevent anastomotic strictures when performing a cervical anastomosis by a CS. Prospective, multicenter RCTs are required to confirm the benefit of using a large-sized CS in patients who undergo cervical esophagogastric anastomosis by a CS.

Acknowledgements The authors would like to thank the members of Department of Gastroenterological Surgery at Aichi Cancer Center Hospital for useful comments and suggestions, and Keitaro Matsuo, MD, PhD, MSc (Division of Cancer Epidemiology and Prevention Aichi Cancer Center Research Institute) for his guidance on statistical analysis.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

References

1. Honda M, Kuriyama A, Noma H et al (2013) Hand-sewn versus mechanical esophagogastric anastomosis after esophagectomy: a systematic review and meta-analysis. Ann Surg 257:238–248. https://doi.org/10.1097/SLA.0b013e31826d4723
2. Kim RH, Takabe K (2010) Methods of esophagogastric anastomoses following esophagectomy for cancer: a systematic review. J Surg Oncol 101:527–533. https://doi.org/10.1002/jso.21510
3. Van Heijl M, Gooszen JA, Fockens P et al (2010) Risk factors for development of benign cervical strictures after esophagectomy. Ann Surg 251:1064–1069. https://doi.org/10.1097/SLA.0b013e3181deb4b7
4. Hayata K, Nakamori M, Nakamura M et al (2017) Circular stapling versus triangulating stapling for the cervical esophagogastric anastomosis after esophagectomy in patients with thoracic esophageal cancer: a prospective, randomized, controlled trial. Surgery (United States) 162:131–138. https://doi.org/10.1016/j.surg.2017.01.013
5. Honkoop P, Siersema PD, Tilanus HW et al (1996) Benign anastomotic strictures after transhiatal esophagectomy and cervical esophagogastrostomy: risk factors and management. J Thorac Cardiovasc Surg 111:1141–1148. https://doi.org/10.1016/S0022-5223(96)70215-5
6. Law S, Suen DTK, Wong KH et al (2005) A single-layer, continuous, hand-sewn method for esophageal anastomosis: prospective evaluation in 218 patients. Arch Surg 140:33–39. https://doi.org/10.1001/archsurg.140.1.33
7. Hanyu T, Kosugi S-I, Ishikawa T et al (2015) Incidence and risk factors for anastomotic stricture after esophagectomy with gastric tube reconstruction. Hepatogastroenterology 62:892–897
8. Ahmed Z, Elliott JA, King S et al (2017) Risk factors for anastomotic stricture post-esophagectomy with a standardized sutured anastomosis. World J Surg 41:487–497. https://doi.org/10.1007/s00268-016-3746-0
9. Wong J, Cheung H, Lui R et al (1987) Esophagogastric anastomosis performed with a stapler: the occurrence of leakage and stricture. Surgery 101:408–415
10. Petrin G, Ruol A, Battaglia G et al (2000) Anastomotic stenoses occurring after circular stapling in esophageal cancer surgery. Surg Endosc 14:670–674
11. West PN, Marbarger JP, Martz MN, Roper CL (1981) Esophagogastrostomy with the EEA stapler. Ann Surg 193:76–81. https://doi.org/10.1097/00000658-198101000-00013
12. Johansson J, Öberg S, Wenner J et al (2009) Impact of proton pump inhibitors on benign anastomotic stricture formations after esophagectomy and gastric tube reconstruction: results from a randomized clinical trial. Ann Surg 250:667–673. https://doi.org/10.1097/SLA.0b013e3181bcb139
13. Yendamuri S, Gutierrez L, Oni A et al (2011) Does circular stapled esophagogastric anastomotic size affect the incidence of postoperative strictures? J Surg Res 165:1–4. https://doi.org/10.1016/j.jss.2010.09.019
14. Johansson J, Zilling T, von Holstein CS et al (2000) Anastomotic diameters and strictures following esophagectomy and total gastrectomy in 256 patients. World J Surg 24:78–84. https://doi.org/10.1007/s002689910015 **(discussion 84–5)**
15. Dindo D, Demartines N, Clavien P-A (2004) Classification of surgical complications: a new proposal with evaluation in a cohort of 6336 patients and results of a survey. Ann Surg 240:205–213
16. Strauss C, Mal F, Perniceni T et al (2010) Computed tomography versus water-soluble contrast swallow in the detection of intrathoracic anastomotic leak complicating esophagogastrectomy (Ivor Lewis): a prospective study in 97 patients. Ann Surg 251:647–651. https://doi.org/10.1097/SLA.0b013e3181c1aeb8
17. Upponi S, Ganeshan A, D'Costa H et al (2008) Radiological detection of post-oesophagectomy anastomotic leak—a comparison between multidetector CT and fluoroscopy. Br J Radiol 81:545–548. https://doi.org/10.1259/bjr/30515892
18. Klein M, Gogenur I, Rosenberg J (2012) Postoperative use of non-steroidal anti-inflammatory drugs in patients with anastomotic leakage requiring reoperation after colorectal resection: cohort study based on prospective data. BMJ 345:e6166. https://doi.org/10.1136/bmj.e6166
19. Bhangu A, Singh P, Fitzgerald JEF et al (2014) Postoperative nonsteroidal anti-inflammatory drugs and risk of anastomotic leak: meta-analysis of clinical and experimental studies. World J Surg 38:2247–2257. https://doi.org/10.1007/s00268-014-2531-1
20. Hakkarainen TW, Steele SR, Bastaworous A et al (2015) Nonsteroidal anti-inflammatory drugs and the risk for anastomotic failure: a report from Washington State's surgical care and outcomes assessment program (SCOAP). JAMA Surg 150:223–228. https://doi.org/10.1001/jamasurg.2014.2239
21. Kotagal M, Hakkarainen TW, Simianu VV et al (2016) Ketorolac use and postoperative complications in gastrointestinal surgery. Ann Surg 263:71–75. https://doi.org/10.1097/SLA.0000000000001260
22. Slim K, Joris J, Beloeil H (2016) Colonic anastomoses and non-steroidal anti-inflammatory drugs. J Visc Surg 153:269–275. https://doi.org/10.1016/j.jviscsurg.2016.06.011
23. Fjederholt KT, Okholm C, Svendsen LB et al (2018) Ketorolac and other NSAIDs increase the risk of anastomotic leakage after surgery for GEJ cancers: a cohort study of 557 patients. J Gastrointest Surg 22:587–594. https://doi.org/10.1007/s11605-017-3623-7
24. Pierie JP, de Graaf PW, Poen H et al (1993) Incidence and management of benign anastomotic stricture after cervical oesophagogastrostomy. Br J Surg 80:471–474
25. Briel JW, Tamhankar AP, Hagen JA et al (2004) Prevalence and risk factors for ischemia, leak, and stricture of esophageal anastomosis: gastric pull-up versus colon interposition. J Am Coll Surg 198:536–541. https://doi.org/10.1016/j.jamcollsurg.2003.11.026
26. Tanaka K, Makino T, Yamasaki M et al (2018) An analysis of the risk factors of anastomotic stricture after esophagectomy. Surg Today 48:449–454. https://doi.org/10.1007/s00595-017-1608-5
27. Cooper GJ, Sherry KM, Thorpe JA (1995) Changes in gastric tissue oxygenation during mobilisation for oesophageal replacement. Eur J Cardiothorac Surg 9:158–160 **discussion 160**
28. Collard JM, Romagnoli R, Goncette L et al (1998) Terminalized semimechanical side-to-side suture technique for cervical

esophagogastrostomy. Ann Thorac Surg 65:814–817. https://doi.org/10.1016/S0003-4975(97)01384-2
29. Orringer MB, Marshall B, Iannettoni MD (2000) Eliminating the cervical esophagogastric anastomotic leak with a side-to-side stapled anastomosis. J Thorac Cardiovasc Surg 119:277–288. https://doi.org/10.1016/S0022-5223(00)70183-8
30. Wang W-P, Gao Q, Wang K-N et al (2013) A prospective randomized controlled trial of semi-mechanical versus hand-sewn or circular stapled esophagogastrostomy for prevention of anastomotic stricture. World J Surg 37:1043–1050. https://doi.org/10.1007/s00268-013-1932-x
31. Price TN, Nichols FC, Harmsen WS et al (2013) A comprehensive review of anastomotic technique in 432 esophagectomies. Ann Thorac Surg 95:1154–1160. https://doi.org/10.1016/j.athoracsur.2012.11.045 **discussion 1160–1**
32. Kondra J, Ong SRY, Clifton J et al (2008) A change in clinical practice: a partially stapled cervical esophagogastric anastomosis reduces morbidity and improves functional outcome after esophagectomy for cancer. Dis Esophagus Off J Int Soc Dis Esophagus 21:422–429. https://doi.org/10.1111/j.1442-2050.2007.00792.x
33. Noshiro H, Urata M, Ikeda O et al (2013) Triangulating stapling technique for esophagogastrostomy after minimally invasive esophagectomy. Surgery (United States) 154:604–610. https://doi.org/10.1016/j.surg.2013.04.007