Superior Thoracic Aperture Size is Significantly Associated with Cervical Anastomotic Leakage After Esophagectomy

Superior thoracic aperture size is significantly associated with cervical anastomotic leakage after esophagectomy

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Abstract

Background: The size of the superior thoracic aperture (STA) may be associated with the incidence of cervical anastomotic leakage after esophagectomy. Using computed tomography (CT) images, we retrospectively investigated relationships between the size of the STA and anastomotic leakage following esophagectomy using the retrosternal or posterior mediastinal reconstruction routes.

Methods: Patients who underwent cervical esophagogastrostomy after esophagectomy between 2009 and 2015 were enrolled in this retrospective study (n=326). The size of the STA was measured at the level of the sternal notch using preoperative CT images, and it was determined as the anteroposterior diameter of the STA minus the diameter of the trachea. Associations between clinical factors, including the size of the STA, and anastomotic leakage were determined.

Results: Anastomotic leakage occurred in 44 patients (13.5%). The size of the STA ranged from 0 mm to 49 mm (median, 16 mm). In univariate analyses, the duration of the operation, tumor location, anastomotic procedure, and the size of the STA were significantly associated with anastomotic leakage. In multivariate analysis, only the size of the STA was independently related to leakage (odds ratio, 1.05; 95% confidence interval, 1.002-1.107; p=0.027). The size of the STA affected the incidence of leakage more frequently with the posterior mediastinal route than with the retrosternal route.

Conclusions: The size of the STA was significantly associated with the incidence of anastomotic leakage after esophagectomy, especially when using the posterior mediastinal route.

Introduction

The prognosis of esophageal cancer is still dismal, and curative surgical resection remains the mainstay even in the present multi-disciplinary treatment era [1, 2]. Esophagectomy is a highly invasive operation, with a high rate of morbidity (41.9-46.0%) [3, 4]. Of the major postoperative complications, anastomotic leakage is common, with an incidence of 13.3-30% [1, 3]. Even today, anastomotic leakage can be troublesome to manage, and it can be fatal [5]. Many risk factors for anastomotic leakage have been investigated, including surgical (anastomotic procedures [6, 7], the reconstruction route [8, 9], and anastomotic site [10]), and patient factors (diabetes [11], preoperative comorbidity [12, 13], blood perfusion of the gastric conduit [14, 15], nutritional status [16], and history of radiation [17]).

Anatomical factors may also affect the risk for anastomotic leakage. Kunisaki et al. previously demonstrated that the size of the superior thoracic aperture (STA) was related to the incidence of anastomotic leakage in patients with cervical anastomosis who had undergone retrosternal route reconstruction [18]. We hypothesized that this relationship would be limited to retrosternal route reconstructions, and it would not exist for patients with posterior mediastinal route reconstructions. Therefore, in the present study, we measured the size of the STA by using preoperative computed tomography (CT) images to test this hypothesis.

Methods

This study was approved by the Cancer Institute Hospital Clinical Research Review Board (Cancer Institute Hospital Ariake, Scientific Review Board No.1762). The requirement for informed consent from patients was waived because of the study's retrospective design.

Between January 2009 and December 2015, 712 patients with esophageal cancer underwent an operation with curative intent at the Department of Gastroenterological Surgery, Cancer Institute Hospital, Tokyo, Japan. Of these, 329 patients received cervical anastomoses by using a gastric conduit following esophagectomy and were eligible for the study. The remaining patients received intrathoracic anastomoses, reconstruction thorough the presternal route, esophagectomy without reconstruction (2-stage esophagectomy), esophagectomy combined with total pharyngolaryngectomy, or reconstruction using the jejunum or colon as a conduit, and thus, were ineligible. Of the 329 eligible patients, three were excluded because of a lack of preoperative CT images. Thus, the final sample consisted of 326 patients (Table 1).

Surgical procedures and neo-adjuvant treatments

Neo-adjuvant treatment was administered to patients with a cStage of IB-III [19]. Rather than chemoradiotherapy, our standard regimen for neo-adjuvant treatment is chemotherapy alone (two courses of cisplatin and 5-fluorouracil) [2].

Eligible patients underwent 3-stage esophagectomy through a right thoracotomy or thoracoscopy with a 2-field or 3-field lymphadenectomy. All patients underwent cervical anastomosis. At our institution, transhiatal or Ivor-Lewis esophagectomy has been rarely performed for thoracic esophageal cancer. A gastric conduit was created using laparotomy or laparoscopic procedures, with a preference for a narrow gastric tube (width, 3.5-4 cm). Most esophago-gastric anastomoses were either performed with two-layers hand-sewn or triangulating stapling anastomoses, using linear staplers [7]. Briefly, hand-sewn anastomosis was performed in the former period (2009-2012); starting in 2013, triangle anastomosis was performed to reduce the incidence of anastomotic leakage and stricture. All patients received jejunostomies or gastrostomies for feeding.

The choice of reconstruction route between the posterior mediastinal and retrosternal routes depended mainly on the period. In the former period (2009-2012), the posterior mediastinal route was preferred. After experiencing three anastomotic tracheal fistulae, the retrosternal route was mainly used because contact between the membranous part of the trachea and anastomosis does not occur through the retrosternal route. Another reason we changed the preferred route concerns small bowel obstruction associated with a jejunostomy. In patients with retrosternal route reconstruction, gastrostomy, instead of jejunostomy, could be performed, potentially decreasing the incidence of small bowel obstruction [20]. For four patients, the reconstruction route was changed intraoperatively from a retrosternal to a posterior mediastinal route because of an extremely narrow cervical space. The head of the left clavicle and manubrium of the sternum were not resected to widen the STA for any patients.

No adjuvant treatment was administered.

Measurement of the size of the STA using CT images

Preoperative CT images with 5-mm slices were taken. Two distances of the STA were measured using preoperative and horizontal CT images: the distance from the ventral surface of the vertebra to the dorsal surface of the sternum at the level of the sternal notch (distance α), and the anteroposterior diameter of the trachea at the same level (distance β) (Fig. 1A and 1B). Distance α minus distance β was obtained to represent the size of the STA.

In addition, for patients with a narrow posterior mediastinal route reconstruction, we correlated leakage with the postoperative anastomotic location relative to the trachea using postoperative CT images because we speculated compression against anastomosis by the trachea and vertebra might cause leakage in patients with a narrow STA. Anastomotic locations were divided into three groups: right side, dorsal side, or left side (Fig. 2A, B, and C, respectively).

Other clinical parameters

Clinical parameters, including anastomotic leakage and the tumor stage (according to the TNM seventh edition classification [19]), were retrieved from our database. Anastomotic leakage was defined as a postoperative complication based on the Clavien-Dindo classification [21]. Patients treated for an anastomotic leakage were considered to have a leakage complication, even if an apparent imaging finding was absent.

Statistical analyses

All statistical analyses were performed using SYSTAT 13 (SYSTAT Software, Inc., Chicago, IL, USA). Associations between clinical factors and the incidence of leakage were analyzed using χ^2 tests for categorical data, and Kruskal-Wallis tests for continuous variables. To remove the effect of confounding factors, variables with a p-value < 0.05 in univariate analyses were included in multivariate logistic regression analysis. To investigate whether the relationship between the size of the STA and the incidence of anastomotic leakage was modified by clinical factors, subgroup analysis was performed. A two-tailed p-value < 0.05 was considered statistically significant.

Results

Patients' characteristics are shown in Table 1. Of 326 patients, 171 (52.5%) received neo-adjuvant chemotherapy, and only 18 (5.5%) underwent neo-adjuvant chemoradiotherapy. Right thoracotomy was performed in 89 patients (27.3%), whereas thoracoscopic esophagectomy was performed in 237 patients (72.7%). The retrosternal reconstruction route (181 patients, 55.5%) was chosen slightly more often than the posterior mediastinal reconstruction route (145 patients, 44.5%). Furthermore, triangulating stapling anastomosis was performed more often (170 patients, 52.1%) than the hand-sewn method (147 patients, 45.1%).

Anastomotic leakage occurred in 44 patients (13.5%), and it was more frequently used during

2009-2013 (33/167, 20.0%) than during 2014-2015 (11/159, 6.9%; p=0.001). Patients with upper-level tumors were more likely to have leakage than patients with middle-level or lower-level tumors (16/71, 22.5%-vs-28/255, 11.0%; p=0.012). With respect to the reconstruction route, leakage rates were similar between the two routes (posterior mediastinal route, 22/145, 15.2%; retrosternal route, 22/181, 12.2%; p=0.428). The use of the triangulating stapling procedure resulted in less leakage than that of hand-sewn anastomoses (13/179, 7.3%-vs-29/147, 19.7%; p=0.005).

The size of the STA ranged from 0 mm to 49 mm, with a median of 16 mm. The size of the STA was significantly associated with leakage (p=0.008), whereby patients with lower values had a higher incidence of leakage (Table 1). To investigate associations between the size of the STA and clinical factors, we divided patients into two groups (patients with a STA < 16 mm vs. those with a STA ≥ 16 mm). There was no statistically significant difference between these two groups (supplementary Table 1).

To evaluate relationships between anastomotic leakage and clinical factors, variables with a p-value < 0.05 in Table 1 were included in multivariate logistic regression analysis. In multivariate analysis, only the size of the STA was significantly related to anastomotic leakage, whereby patients with lower values had a higher risk of leakage (odds ratio [OR], 1.05; 95% confidence interval [CI], 1.002-1.107; p=0.027). Other clinical factors, including the duration of the operation, tumor location, or anastomotic procedure, were not significantly related to the incidence of leakage (Table 2).

Additionally, we investigated relationships between the size of the STA and anastomotic leakage for each reconstruction route. For either route, patients with lower STA values were more likely to develop leakage. Contrary to our expectations, this tendency was more common for the posterior mediastinal route (OR, 1.072; 95% CI, 1.001-1.148; p=0.046) than for the retrosternal route (OR, 1.042; 95% CI, 0.97-1.12; p=0.26) (Fig. 3).

For the 39 patients with low STA values (≤ 9 mm, the first quartile) and reconstruction through the posterior mediastinal route, we examined whether the anastomosis site was related to leakage by using postoperative CT images (Fig. 2). Of 7 patients with anastomosis on the right side of the trachea, only 1 had leakage (14%). In contrast, of 32 patients with anastomosis on the dorsal or left side of the trachea, 9 had leakage (28%). However, this difference was not statistically significant (p=0.448).

Finally, we performed a subgroup analysis to investigate whether the relationship between the size of the STA and the incidence of anastomotic leakage was modified by clinical factors (Fig. 3). Body mass index (BMI) of ≥20-25kg/m^2 was identified as a significant modifier (P for interaction=0.007). Other clinical factors, including sex, age, anastomotic procedure, or reconstruction route, did not affected the relationship between the size of the STA and anastomotic leakage (Fig. 3).

Discussion

The present study demonstrated that the size of the STA, as represented by the anteroposterior diameter of the STA minus the diameter of the trachea, was an independent risk factor for anastomotic leakage in cervical esophagogastrostomy following esophagectomy. Contrary to our expectations, the relationship seemed stronger for the posterior mediastinal route rather than for the retrosternal route.

At the beginning of the present study, we measured the retrosternal space area using a freehand measuring tool for CT images. However, values obtained by this method were influenced by the location of the carotid artery or innominate vein, which was obscure. In addition, these values were not significantly related to leakage. This was at least partly because this method did not give weight to the diameter of the trachea or the space between the vertebra and trachea. As the diameter of the trachea and space between the vertebra and trachea affects the area of the STA and a large trachea is more likely to make the gastric conduit narrower, we used a value equal to the anteroposterior diameter of the STA minus the diameter of the trachea. Thus, we consider that our procedure is simpler and more distinct than that used in the previous procedure[18].

We had hypothesized that the size of the STA would not affect the risk for anastomotic leakage with posterior mediastinal route reconstruction, but it would affect the risk with retrosternal route reconstruction because western experts have often suggested the necessity of resection of the head of the left clavicle and manubrium of the sternum only with retrosternal route reconstruction [22]. However, we found that the risk for anastomotic leakage was influenced more by the size of the STA when using the posterior mediastinal route. Furthermore, patients with anastomosis on the dorsal or left side of the trachea had about twice as much leakage as those with anastomosis on the right side of the trachea; this difference was not statistically significant, possibly because of the low number of patients with a narrow STA (39 patients). With a dorsal or left-sided anastomosis, we speculate that the tip of the gastric conduit is compressed by the trachea, vertebrae, or cervical artery, which would lead to poor blood perfusion at the anastomosis site (Fig. 2B and 2C) [15, 17, 23].

According to analyses of P for interaction (Fig. 3), the presence of cervical anastomotic leakage was likely to be more influenced by the size of the STA in younger patients or patients with a moderate BMI (20-25 kg/m^2). We speculate that patients without co-morbidity or nutritional risk could be affected by the size of the STA. In other words, elderly, lean, or obese patients could have other risk factors affecting anastomosis, including cardiovascular disease, pulmonary disease, diabetes, or malnutrition, and these factors may be more of an indicator of anastomotic leakage than the size of the STA.

To avoid anastomotic leakage in patients with a narrow STA, intrathoracic anastomosis can be chosen. To avoid congestion of the anastomosis, the anastomosis itself can be pressed into the right thorax after anastomosis through the posterior mediastinal route. In addition, resection of the head of the left clavicle and manubrium of the sternum must be alternative although it is very uncommon in Japan.

The present study has some limitations. First, the study had a retrospective nature. Second, several kinds of surgical procedures and durations of operation were included. However, even in this diverse cohort of patients, the size of the STA was identified as an independent indicator of anastomotic leakage in multivariate analysis.

In conclusion, we found that the anteroposterior diameter of the STA minus the diameter of the trachea was significantly associated with the incidence of anastomotic leakage after esophagectomy, especially when using the posterior mediastinal route.

Disclosure

The authors have no conflicts of interest to declare.

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Table 1. Relationships between patients' characteristics and anastomotic leakage.

		No. of patients		
		Total	Anastomotic leakage	
		N=326	N=44 (13.5%)	*p*-value
Period				
	2009-2013	167	33 (20.0%)	0.001 †
	2014-2015	159	11 (6.9%)	
Sex				
	Male	274	39 (14.2%)	0.372
	Female	52	5 (9.6%)	
Age (years; median, range)				
		64 (41-82)	63 (47-78)	0.157
Histological types				
	SCC	299	39 (13.0%)	0.669
	Adenocarcinoma	23	4 (17.4%)	
	Other	4	1 (25%)	
BMI (kg/m^2; median, range)				
	<20	45	7 (15.6%)	0.212
	20-25	233	27 (11.6%)	
	≥25	48	10 (20.8%)	
Cardiovascular disease				
	Absent	187	26 (13.9%)	0.803
	Present	139	18 (12.9%)	
Diabetes mellitus				
	Absent	288	37 (12.8%)	0.345
	Present	38	7 (18.4%)	
Albumin level (g/dL; median, range)				
		4.1 (2.8-5.1)	4.1 (2.8-5.1)	0.709
Tumor location				

	Upper	71	16 (22.5%)	0.012 †
	Middle or lower	255	28 (11.0%)	
cT1234				
	cT1 or T2	201	30 (14.9%)	0.338
	cT3 or T4	125	14 (11.2%)	
cN0123				
	cN0	175	29 (16.6%)	0.08
	cN1, N2, or N3	151	15 (9.9%)	
Neo-adjuvant treatment				
	Absent	137	19 (13.9%)	0.867
	Present	189	25 (13.2%)	
Approach				
	Right thoracotomy	89	14 (15.7%)	0.47
	MIE	237	30 (12.7%)	
Reconstruction route				
	Posterior mediastinal	145	22 (15.2%)	0.428
	Retrosternal	181	22 (12.2%)	
Anastomotic procedure				
	Triangulating	170	13 (7.6%)	0.005 †
	Hand-sewn	147	29 (19.7%)	
	Other	9	2 (22.2%)	
Size of the STA				
		16 (0-49)	12.5 (4-36)	0.008 †

SCC, squamous cell carcinoma; BMI, body mass index; MIE, minimally invasive esophagectomy; STA, superior thoracic aperture; † $p < 0.05$

Table 2. Associations between clinical factors and anastomotic leakage using the logistic regression test

Variable	Multivariate analysis			Univariate analysis	
	Odds ratio	95 % CI	*p*-value	Odds ratio	*p*-value
Period					
2009-2013 vs. 2014-2015	2.3	0.8-6.8	0.127	3.3	0.001[†]
Tumor location					
Upper vs. middle and lower	1.9	0.9-3.9	0.085	2.4	0.014[†]
Anastomotic procedure					
Triangulating vs. other	0.8	0.3-2.2	0.61	0.3	0.002[†]
Size of the STA					
	1.05	1.002-1.107	0.027[†]	1.06	0.019[†]

CI, confidence interval; STA, superior thoracic aperture; † $p < 0.05$

Figure Captions

Fig. 1

Schematic illustration of the superior thoracic aperture (STA)

Arrows with dotted lines (α): distance from the ventral surface of the vertebra to the dorsal surface of the sternum at the level of the sternal notch.

Arrows with continuous lines (β): anteroposterior diameter of the trachea at the sternal notch.

The value of the anteroposterior diameter in the STA minus the diameter of the trachea equals distance α minus distance β (mm).

1A: A patient with a narrow STA of 3 mm.

1B: A patient with a wide STA of 33 mm.

Fig. 2

Postoperative anastomotic locations on computed tomography images for patients with a narrow STA.

1A: A patient with right-sided anastomosis

1B: A patient with dorsal-sided anastomosis

1C: A patient with left-sided anastomosis

STA, superior thoracic aperture

Fig. 3

A forest plot showing odds ratio of the incidence of anastomotic leakage on the size of the STA in each subgroup analysis.

BMI, body mass index; CI, confidence interval; †$p < 0.05$

Fig. 1A

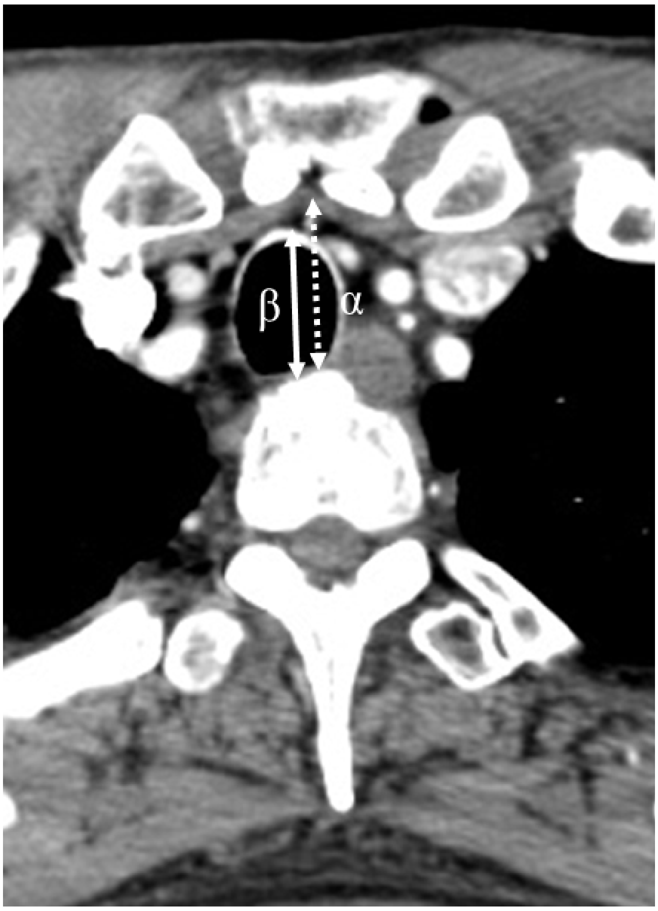


Fig. 1B

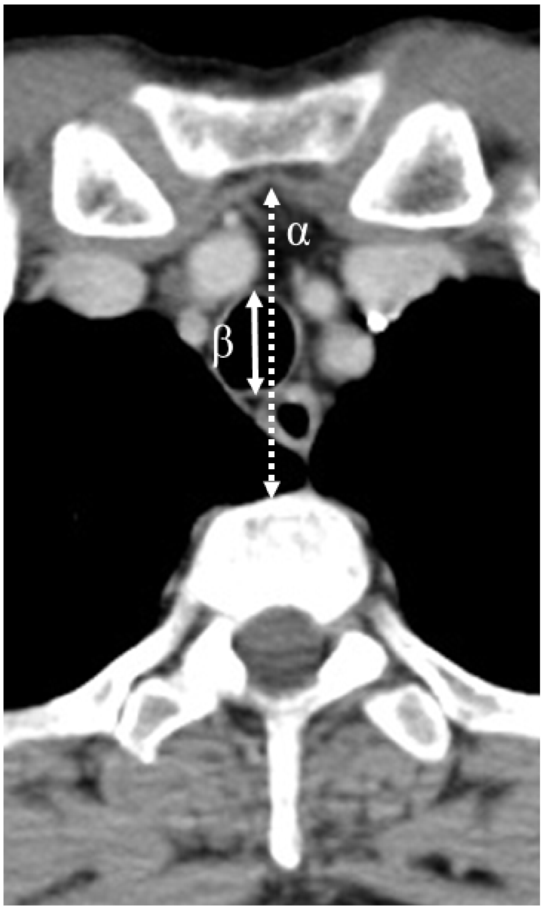
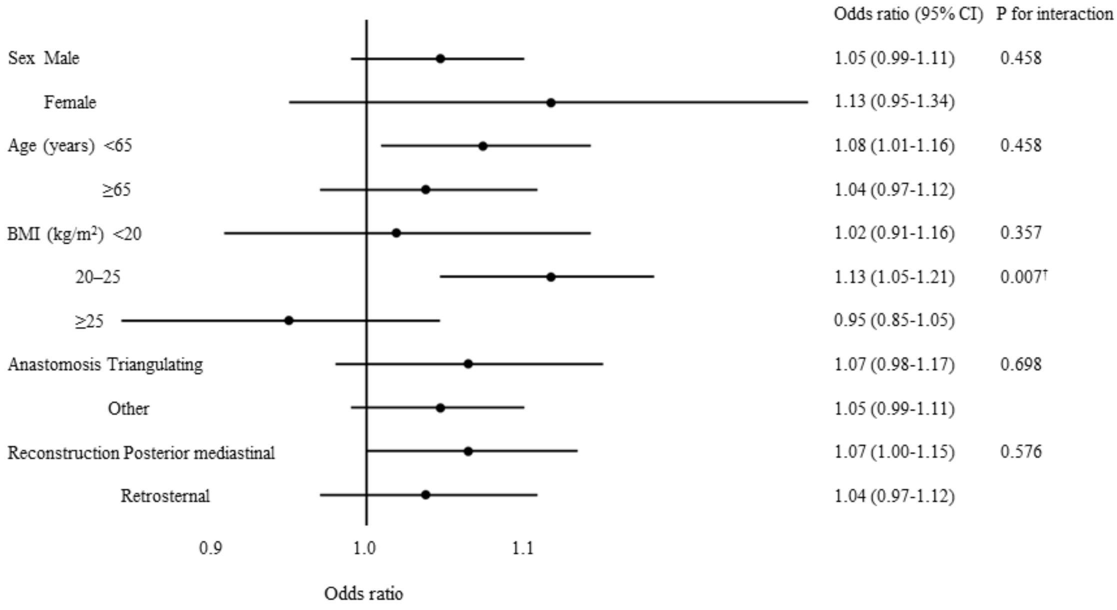


Fig. 2A

Fig. 2B

Fig. 2C

Fig. 3


Odds ratio (95% CI)
P for interaction
Sex Male
1.05 (0.99-1.11)
0.458
Female
1.13 (0.95-1.34)
Age (years) <65
1.08 (1.01-1.16)
0.458
≥65
1.04 (0.97-1.12)
BMI (kg/m2) <20
1.02 (0.91-1.16)
0.357
20–25
1.13 (1.05-1.21)
0.007†
≥25
0.95 (0.85-1.05)
Anastomosis Triangulating
1.07 (0.98-1.17)
0.698
Other
1.05 (0.99-1.11)
Reconstruction Posterior mediastinal
1.07 (1.00-1.15)
0.576
Retrosternal
1.04 (0.97-1.12)
0.9
1.0
1.1
Odds ratio

Supplementary Table 1 Relationships between patients' characteristics and the size of the STA.

	Number of patients		
	STA<16	STA≥16	
	N=155	N=171	*p*-value
Sex			
Male	132	142	0.602
Female	23	29	
Age (years; median, range)			
	64 (43-82)	64 (41-82)	0.291
BMI (kg/m^2; median, range)			
<20	19	26	0.302
20-25	117	116	
≥25	19	29	
Tumor location			
Upper	36	35	0.547
Middle or lower	119	136	
Reconstruction route			
Posterior mediastinal	77	68	0.072
Retrosternal	78	103	
Anastomotic procedure			
Triangulating	75	95	0.196
Other	80	76	

STA, superior thoracic aperture, BMI, body mass index