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**Manuscript title:**

Laparoscopic creation of a retrosternal route for gastric conduit reconstruction

**Brief title:** Laparoscopic creation of a retrosternal route**Authors and their affiliations:**

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7

## ABSTRACT

### Background

Retrosternal reconstruction is associated with a lower risk of mediastinitis, gastro-tracheal fistula, and hiatal hernia. Historically, traumatic manual creation of the retrosternal tunnel has been performed using one's fist. We report a novel and atraumatic laparoscopic procedure to create the retrosternal route.

### Methods

We have laparoscopically created the retrosternal route in 25 thoracoscopic, mediastinoscopic, or robot-assisted minimally invasive esophagectomies since August 2019. Specifically, a peritoneal incision is started at the dorsal side of the xiphoid process. Through a 12-mm port inserted slightly to the right of and superior to the umbilical camera port, we dissect loose connective tissues from the caudal to the cranial side using behind the sternum and inside the internal thoracic vessels as landmarks. The time required to create the route was calculated. Then, the cumulative sum (CUSUM) method and the simple moving average of five cases were used to evaluate the learning curve of this novel procedure. Operative outcomes were analyzed according to the learning curve results and also compared with 25 cases of post mediastinal reconstruction counterparts.

### Results

Twenty-five patients were divided into the early group (six patients) and late group (19 patients) based on the peak of the CUSUM chart. The time required for route creation was 28.5 minutes (median) in the early and 15 minutes in the late group, indicating a significant

1 difference ( $P=0.038$ ). The overall incidence of pleural injury was 20% (five of 25 patients),  
2 with no significant difference between the groups. There was no significant difference in the  
3 incidence of perioperative complications. Also, there were no significant differences in  
4 perioperative complications, or gastric conduit functions one year after surgery between the  
5 retrosternal and the post mediastinal reconstruction.

## 6 7 **Conclusions**

8 Laparoscopic creation of a retrosternal route for gastric conduit reconstruction is safe and  
9 feasible and has a short learning curve.

10  
11 **Key words:** minimally invasive esophagectomy (MIE), robot-assisted MIE (RAMIE),  
12 retrosternal route, gastric conduit reconstruction, learning curve

## Introduction

After esophagectomy, reconstruction can be performed using a subcutaneous, retrosternal, or posterior mediastinal route<sup>1,2</sup>. Each has its advantages and disadvantages, with methods of construction that vary among institutes worldwide. The posterior mediastinal route has the advantage of enabling physiological food flow<sup>3,4</sup>, but it is also associated with a relatively high risk of fatal complications such as mediastinitis, gastro-tracheal fistula, and hiatal hernia<sup>5,6</sup>. In comparison, the retrosternal route uses a shorter tunnel and is less likely to cause inflammatory complications in the posterior mediastinum<sup>7</sup>. Traditionally, route creation has been performed blindly and manually under laparotomy, but the procedure is rather traumatic and carries a relatively high risk of bleeding or pleural injury<sup>8</sup>. In this study, we propose and evaluate the usefulness of a laparoscopic retrosternal route creation (LRRC) method and define the learning curve after its introduction using the cumulative sum (CUSUM) method. Also, we compared surgical outcomes between 25 retrosternal reconstruction cases and 25 posterior mediastinal of that.

## Patients and methods

### *Patient population*

We introduced LRRC in August 2019, and from then until September 2020, we used it in 25 cases. All involved minimally invasive esophagectomy (MIE), including robot-assisted, thoracoscopic, and mediastinoscopic approaches. The triangulating stapling technique for cervical esophagogastric anastomosis was used in all cases<sup>9</sup>. Patients' preoperative characteristics are shown in Table 1. To compare the surgical outcomes, we reviewed the most recent 25 cases of post mediastinal reconstruction performed between November 2018 and

1 August 2019. These patients' preoperative characteristics are also shown in Table 1. The ethics  
2 review boards of Kobe University Hospital approved the study design.

### 3 4 *Surgical procedure*

#### 5 •*Before the procedure*

6 After the thoracic portion of the operation was completed in a minimally invasive manner  
7 (robot-assisted, thoracoscopic, or mediastinoscopic), ports were placed as shown in Fig. 1, then  
8 the abdominal portion of the operation was performed laparoscopically. As was standard, the  
9 right gastric artery and right gastroepiploic artery and vein were preserved when gastric  
10 regional lymphadenectomy was performed. The left gastric artery and vein, left gastroepiploic  
11 artery and vein, and short gastric artery were dissected. The distal portion of the esophagus was  
12 detached in the thoracic cavity and then pulled into the abdominal cavity through the hiatus.  
13 The esophageal hiatus was then closed with non-absorbable 2-0 V-Loc™ PBT.

#### 14 15 •*Entry*

16 The falciform ligament of the liver was cut sharply on the cranial side. Then, a 23-G needle  
17 was inserted through the abdominal wall at the caudal point of the xiphoid as a landmark. This  
18 23-G point was used as the landmark for beginning the peritoneal incision, and the sternal  
19 portion of the diaphragm and the transversus abdominis muscle originated from here. The  
20 fasciae of these muscles had to be consciously incised to correctly enter the posterior space  
21 behind the sternum (Fig. 2a). These steps were important because if the incision was initiated  
22 in the wrong location, it could easily be improperly continued towards the pericardium or  
23 bilateral pleura. Expanding the entry hole laterally (by about 5cm widths or more) could

facilitate the subsequent steps. In this regard, we usually consider the full opening widths of forceps as about 2.5cm, so we take two full open widths of forceps as a guide.

#### *•Creating the retrosternal route with an energy device*

Using the posterior surface of the sternum and the internal thoracic blood vessels as landmarks, the relatively sparse connective tissue on the ventral epicardial surface was dissected cranially with an energy device (e.g., Ligasure®) (Fig. 2b). The transversus thoracis muscles originate from both sides of the sternum, and internal thoracic arteries and veins run along the ventral sides of these muscles. Under laparoscopic observation, the presence or absence of slight bleeding and pleural injury could be clearly seen. If the pleura is injured, postoperative herniation of the reconstructed gastric conduit may occur in the thoracic cavity; therefore, it is crucial to perform a visual laparoscopic examination to prevent pleural injury. While performing blunt dissection, as in manual route creation, the tissue that remained in the form of streaks was cauterized with the energy device. If bleeding occurred, it was possible to perform immediate hemostasis without changing the forceps.

#### *•Completion of route creation*

The total operation time could be shortened by approaching from the neck concomitantly with laparoscopic route creation. We usually make a collar-shaped incision on the left front of the neck and take sternohyoid and sternothyroid myotomy at their origins of the sternum. Then we gently dissected the layer behind the jugular notch with fingers or a metal spatula. If the laparoscopic route creation was sufficiently complete, this maneuver could be visually confirmed with the laparoscope (Fig. 2c). We usually do not remove the sternoclavicular joint

or do manubrium resection but carefully and sufficiently broaden behind the jugular notch for about 5cm or more width to avoid the postoperative obstruction of conduit around there.

Dissection from the caudal and cranial sides was continued until complete, at which point the retrosternal route creation was finished. Then, the tape inserted via the cervical wound to raise the gastric conduit was grasped laparoscopically and pulled toward the abdominal cavity (Fig. 2d, Video).

#### *Evaluation of the procedure learning curve using the CUSUM method and a simple moving average (SMA) chart*

The time from the initial peritoneal incision to the completion of the retrosternal space dissection was defined as the time required for route creation. The route creation time in 25 cases was visualized using the CUSUM method and the SMA of five cases (5-SMA), and the number of cases required for stabilization of procedure time was determined. The CUSUM method is a sequential analysis technique that is widely used for monitoring change detection<sup>10,11</sup>. The CUSUM is shown as the total sum of the sequential difference of a particular parameter between each case and the mean value of all cases. In this study, the parameter used for CUSUM was the route creation time. The SMA smooths out short-term fluctuations; thus, it can be used to show the end of the learning phase where there is flattening of the curve<sup>12</sup>. Based on the order in which operations were performed, the patients were divided into early and late groups, and short-term outcomes were compared.

#### *Evaluation of the functionality of the retrosternal gastric conduit*

In addition to short-term surgical outcomes, we evaluated the gastric conduit function. To

1 achieve this, we used regurgitation findings (Los Angeles Classification) by  
2 esophagogastroduodenoscopy (EGD) approximately one year after the surgery and the  
3 presence or absence of gastric conduit stenosis requiring dilatation along with the clinical  
4 symptoms. Cases for which EGD results were not available due to death, recurrence, or time  
5 not reached were excluded (shown as Not Available). We compared these 25 retrosternal case  
6 series with the 25 most recent posterior mediastinal route reconstruction cases.

### 8 *Statistical analysis*

9 Continuous variables were assessed using Student's t-test or Wilcoxon's rank-sum test as  
10 appropriate, and categorical variables were evaluated using Fisher's exact test. P values less  
11 than 0.05 were considered statistically significant. R (version 4.0.0) was used for statistical  
12 analysis (R Core Team (2020). R Foundation for Statistical Computing, Vienna, Austria).

## 14 **Results**

### 15 *Learning curve evaluation using CUSUM and 5-SMA charts*

16 On the CUSUM chart, an obvious peak was observed in the fifth case, with a stable decline  
17 thereafter (Fig. 3). Based on this result, we assumed that around the sixth case was the plateau  
18 of the learning curve. The 5-SMA chart showed a gradual decline from the beginning and  
19 remained almost constant beginning with the 10th case (Fig. 4).

### 21 *Surgical outcomes of the early/late groups*

22 Based on the results of the CUSUM chart, statistical analysis was performed by categorizing  
23 the first to sixth patients into the early group and the seventh and subsequent patients into the

late group. The characteristics of both groups are shown in Table 2. There were no significant differences between the two groups in terms of age, gender, height, weight, preoperative therapy, type of MIE (robot-assisted/thoracoscopic/mediastinoscopic), stage, or **Charlson Comorbidity Index**. Comparisons of outcomes between the two groups are shown in Table 3. The route creation time was significantly shorter in the late group, but the total operation time was significantly longer. Prolonged total time might be attributable to more cases of RAMIE in the late group. There were no differences in blood loss, histological type, the rates of pleural injury, anastomotic leakage, or other complications. In addition, there was no significant difference in the length of postoperative hospital stay (Table 3).

#### *Surgical outcomes and the conduit functionality of the retrosternal route and the posterior mediastinal route*

The preoperative characteristics of both groups are shown in Table 1. There were no significant differences between the two groups in terms of age, height, weight, preoperative therapy, stage, or Charlson Comorbidity Index. RAMIE cases were more common in the retrosternal group, and significantly more males were present in the post mediastinal group. Comparisons of outcomes between the two groups are shown in Table 4. There were no differences in blood loss, histological type, anastomotic leakage, other complications, or the length of postoperative hospital stay. The total operation time was significantly longer in the retrosternal group, but this might be attributed to more RAMIE cases. There were no significant differences in LA classification and conduit stenosis between the groups regarding gastric conduit function.

## Discussion

Compared to blind, manual route creation, LRRC is easier to perform and results in the improved visual observation of the left and right parietal pleura, internal thoracic blood vessels, and penetrating branches on the posterior side of the sternum. In addition, even if there is bleeding, it is easy to keep the reconstruction route dry by accurately identifying the bleeding point and performing reliable hemostasis. Although it was difficult to determine the exact amount of blood loss during route creation in this study, it was visually lower in the late group than in the early group.

In this study, five of 25 patients experienced a pleural injury during LRRC. In two patients, the pleural injuries occurred at the first peritoneal incision, caused by incorrect entry into the thoracic cavity due to peritoneal incision slightly posterior to the sternum. It was easy to identify pleural injuries under laparoscopic observation, and those were repaired with sutures. In order to avoid pleural injury at this point, it is necessary to make sure that the liver side of the previously dissected falciform ligament is sufficiently towed to reach the dorsal side of the sternum. The pleural injuries in the other three patients occurred in route creation, and two of them were so small (about the size of a pinhole) that repair was not performed. The other one was repaired with sutures. In fact, during blind, manual route creation, more serious injuries may be more likely.

Regarding the learning curve, the CUSUM chart demonstrated a peak at the fifth case. The 5-SMA chart was stable beginning at the 10th case, but there was a large difference between cases until the sixth case, with little variation thereafter. Due to the nature of the SMA chart, the point at which stability is obtained is shifted rightward by the number of samples to be averaged from the point where there is less variation between samples. From this point of

view, it is considered that the learning curve peaked at about five or six cases, which is consistent with the results of the CUSUM method. Thus, it is considered that LRRC can be learned relatively quickly and easily in facilities where staff are familiar with laparoscopic surgery.

Surgical resection is still the standard treatment for advanced esophageal cancer, and reports of reconstructed gastric tube cancer are not uncommon<sup>13</sup>.

Partial, subtotal, or total gastric conduit resection is indicated when endoscopic treatment is difficult, but adhesion around the reconstructed gastric conduit may be problematic in such cases<sup>14</sup>. Controlling bleeding as much as possible during retrosternal route creation may contribute to reducing adhesions around the reconstructed gastric conduit during the subsequent reoperation, as described above.

The main limitations of this study were its single-center design and the small number of cases. We plan to accumulate further cases and report additional follow-up data in the future, including more specific comparisons with post mediastinal reconstruction cases.

1    **Author contributions**

2    Study conception and design: Horikawa, Oshikiri, Nakamura

3    Acquisition of data: Horikawa, Oshikiri, Takiguchi, Urakawa, Hasegawa, Nakamura

4    Analysis and interpretation of data: Horikawa, Oshikiri, Yamamoto, Yamashita, Matsuda T

5    Video editing: Horikawa, Oshikiri, Kanaji, Matsuda Y

6    Drafting of manuscript: Horikawa, Oshikiri, Suzuki

7    Critical revision: Horikawa, Oshikiri, Kakeji

8    All authors belong to Kobe University read and approved the final manuscript.

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1    **Disclosures:**

2    Drs. Manabu Horikawa, Taro Oshikiri, Gosuke Takiguchi, Naoki Urakawa, Hiroshi Hasegawa, Masashi

3    Yamamoto, Shingo Kanaji, Yoshiko Matsuda, Kimihiro Yamashita, Takeru Matsuda, Tetsu Nakamura,

4    Satoshi Suzuki, and Yoshihiro Kakeji have no conflicts of interest or financial ties to disclose.

5

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- 15

## Figure legends

### •Figure 1

Port placement. Five ports are placed in the abdominal wall. The 12-mm port slightly to the right of and superior to the umbilical camera port is mainly used for dissection.

### •Figure 2

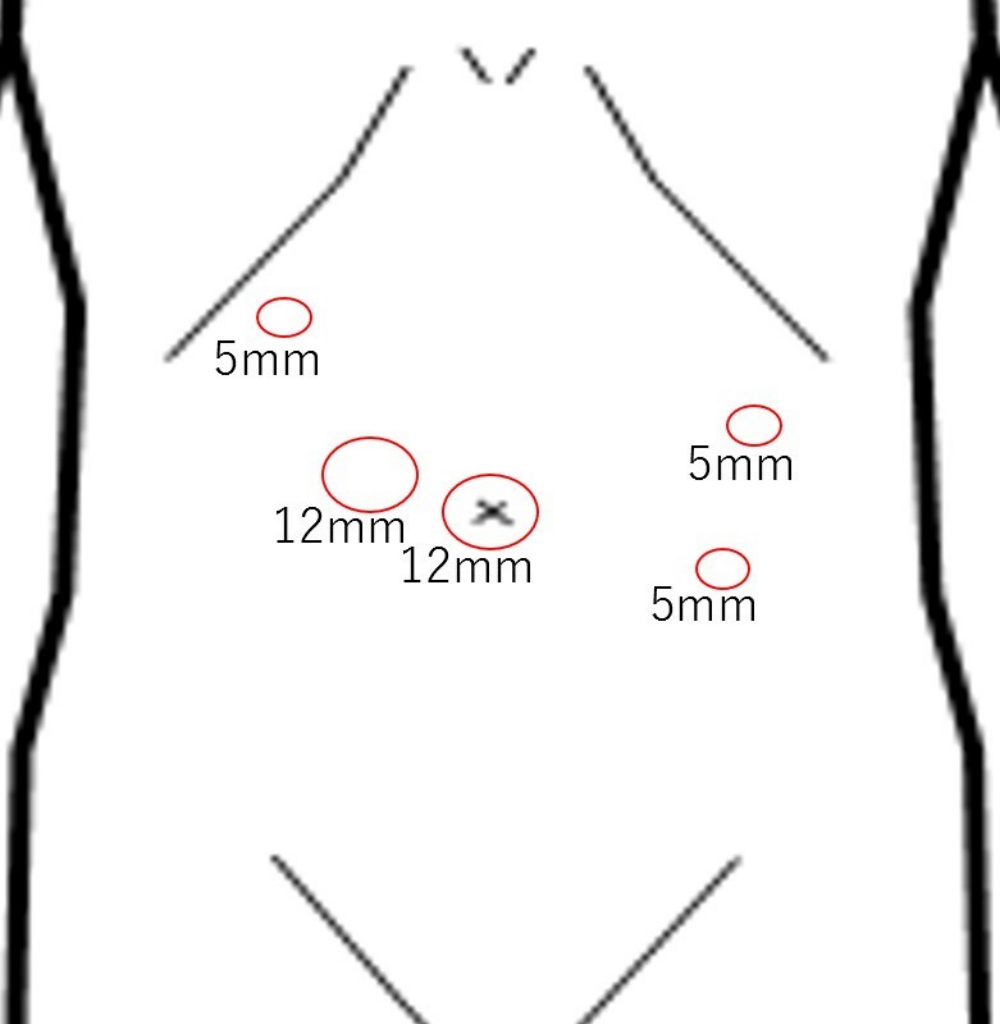
Retrosternal route creation. a) The fasciae of the diaphragm and transversus abdominis muscle are cauterized to enable entry into the retrosternal space. b) Sparse connective tissue is dissected with an energy device, with the dorsal sternum and the internal thoracic blood vessels used as landmarks. c) A surgical approach from the neck performed concomitantly with laparoscopic route creation can shorten the operation time. d) A string inserted through the neck is pulled toward the abdominal cavity laparoscopically.

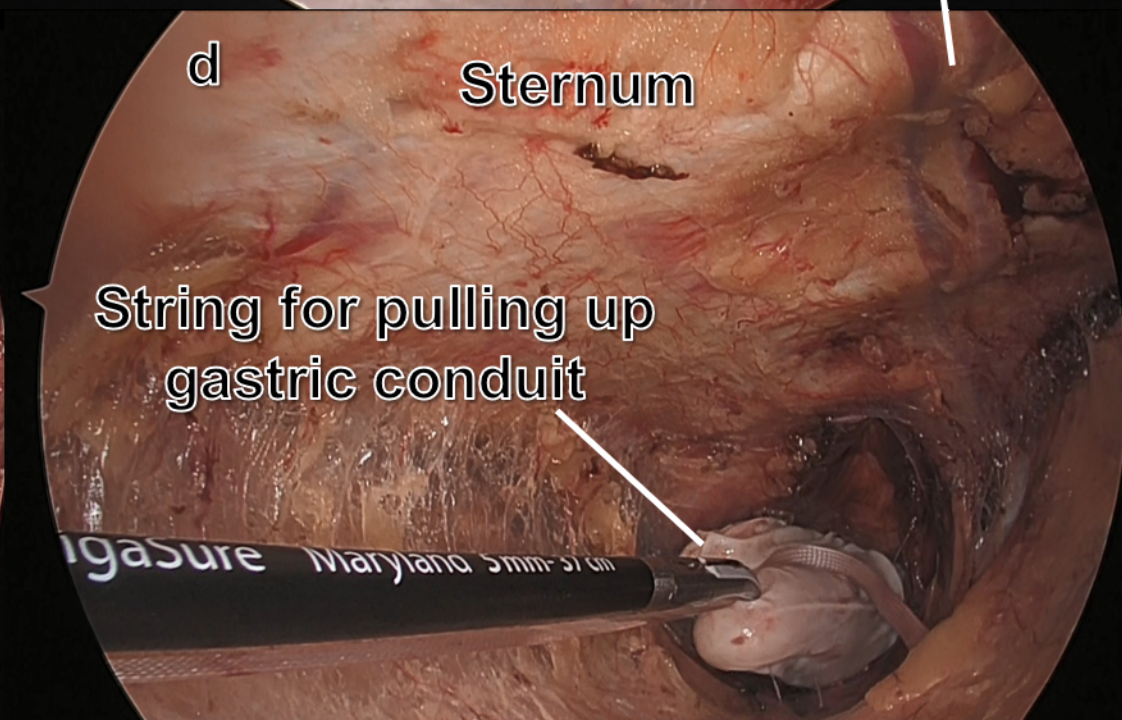
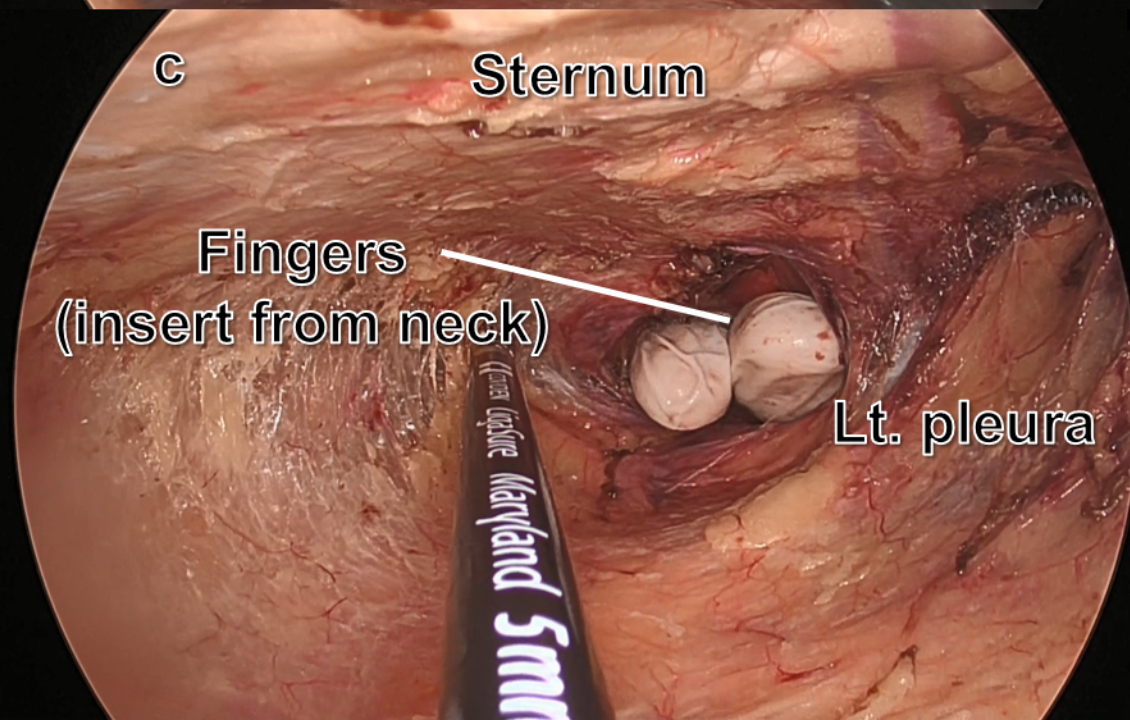
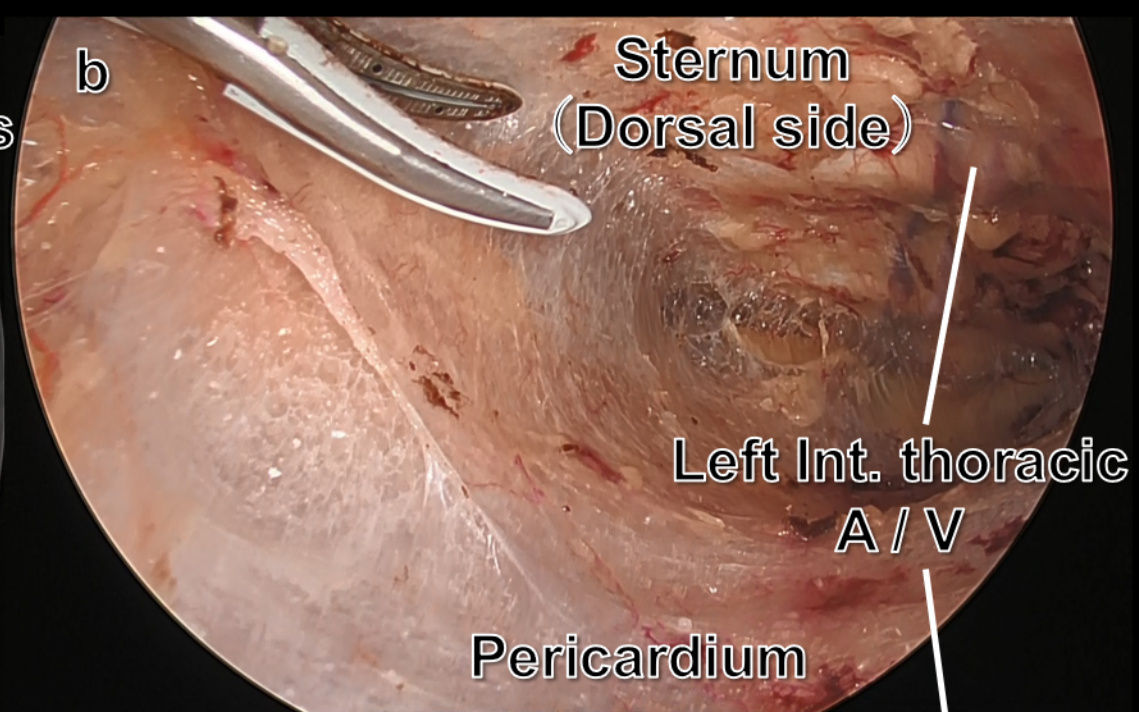
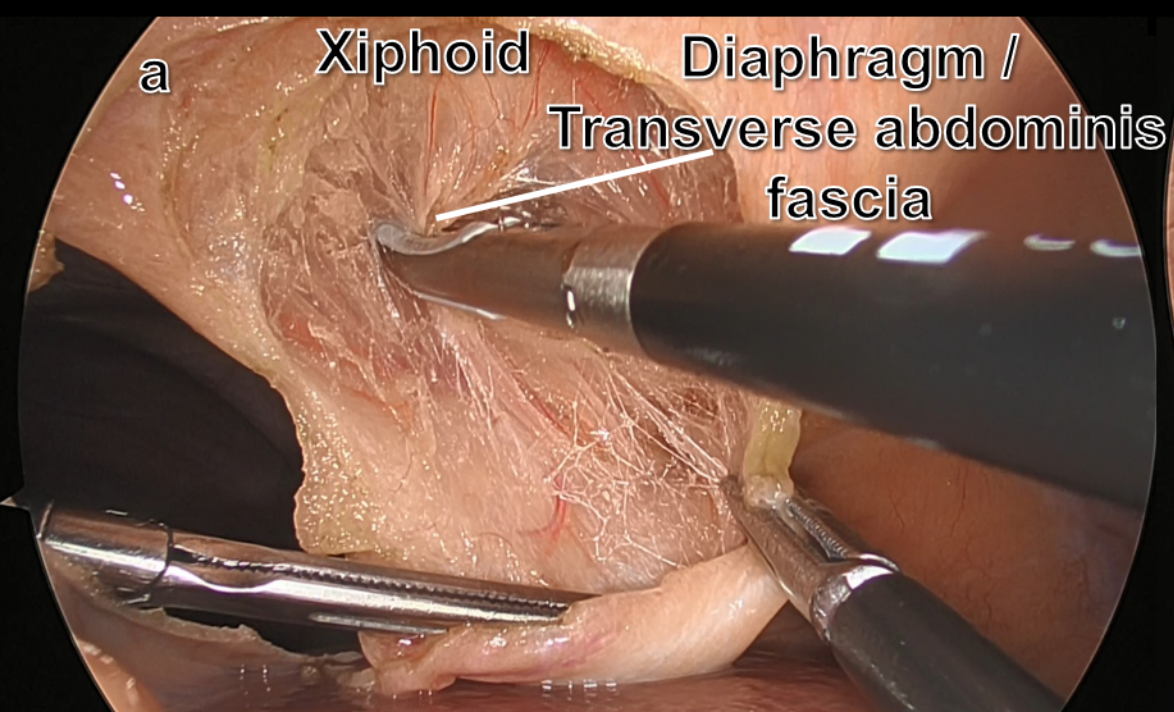
### •Figure 3

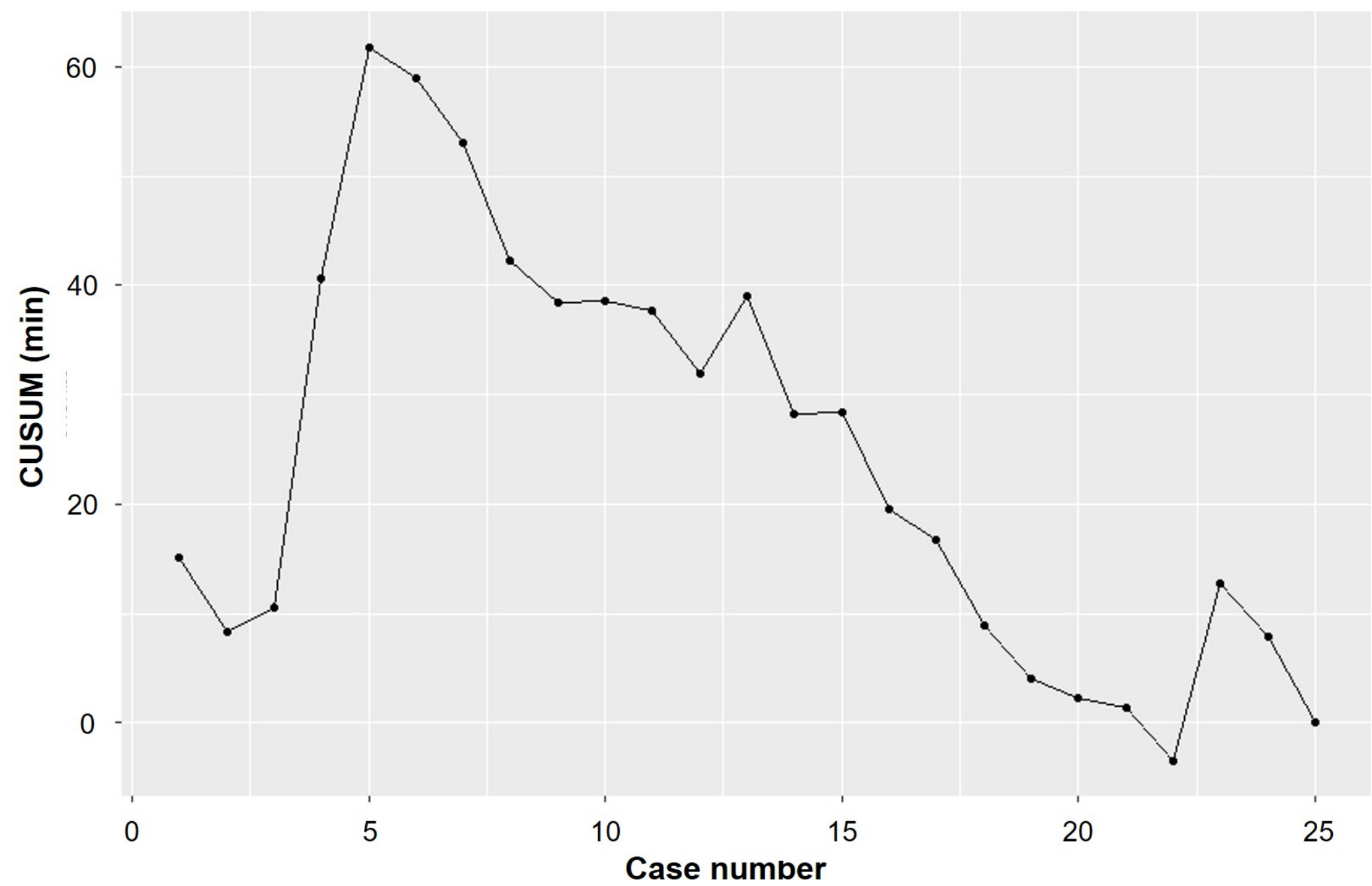
CUSUM chart for the route creation time. There is an obvious peak at the fifth case, and the sequential decline implies that the sixth case is the plateau of the learning curve.

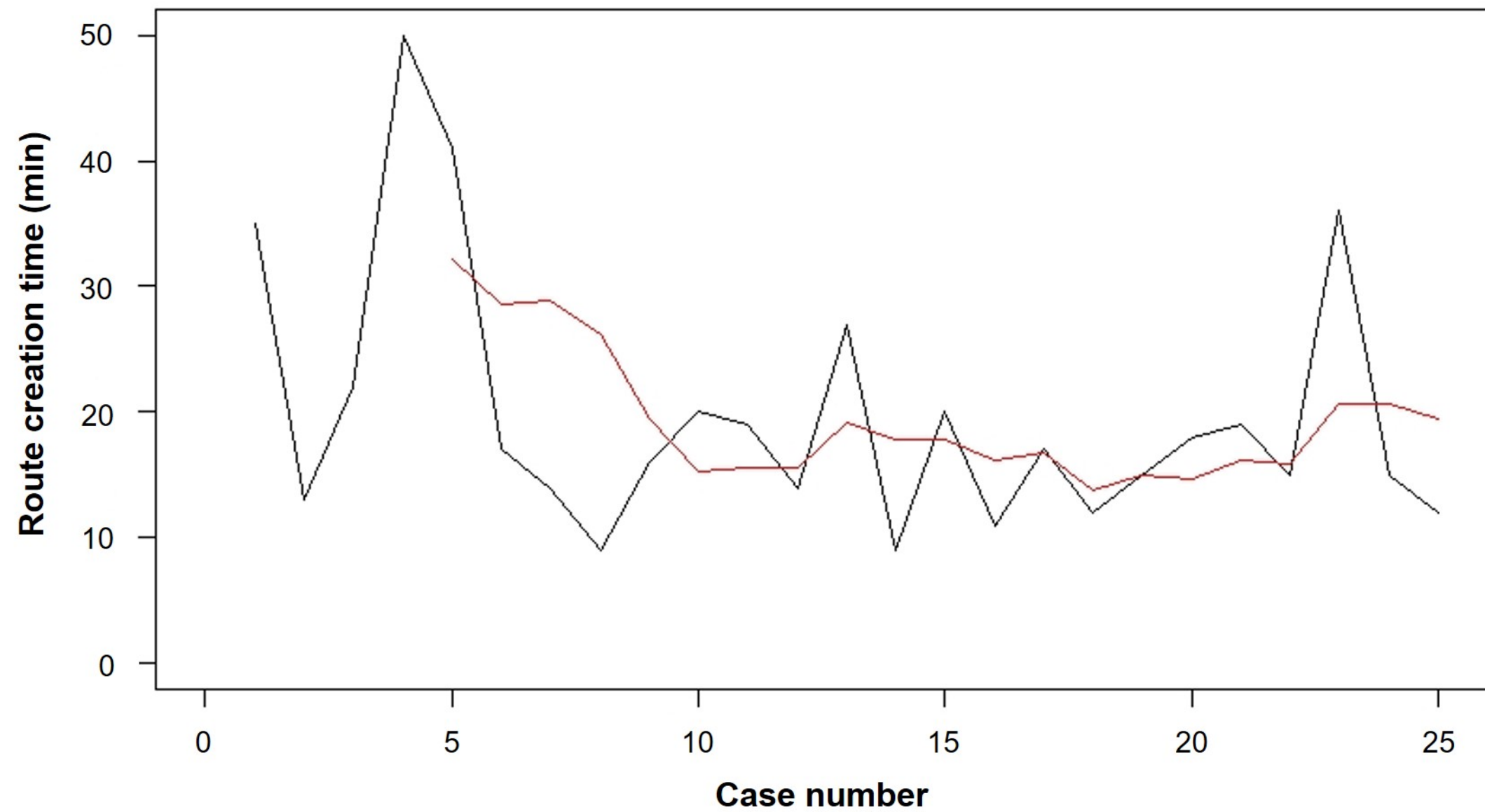
### •Figure 4

5-SMA chart for the route creation time. There is a gradual decline from the beginning, with minimal change after the 10th case.









1 Table 1. Demographic and clinical characteristics of all patients

Reconstruction route	Retrosternal (n = 25)	Posterior mediastinal (n = 25)	P
Age	67.7 ± 9.9	65.5 ± 9.8	0.443 <sup>a)</sup>
Gender			0.012 <sup>b)</sup>
Male / Female	13 (52%) / 12 (48%)	22 (88%) / 3 (12%)	
Height (cm)	163.3 ± 8.7	166.1 ± 8.8	0.257 <sup>a)</sup>
Weight (kg)	57.4 ± 9.5	62.8 ± 12.3	0.092 <sup>a)</sup>
Preoperative therapy			1.000 <sup>b)</sup>
NAC / NACRT / None	13 (52%) / 0 (0%) / 12 (48%)	12 (48%) / 0 (0%) / 13 (52%)	
RAMIE / Thoracoscopic / Mediastinoscopic	19 (76%) / 5 (20%) / 1 (4%)	6 (24%) / 19 (76%) / 0 (0%)	<0.001 <sup>b)</sup>
UICC-cStage			0.358 <sup>b)</sup>
0	1 (4%)	1 (4%)	
I	6 (24%)	11 (44%)	
II	5 (20%)	2 (8%)	
III	10 (40%)	6 (24%)	
IV	3 (12%)	5 (20%)	
Charlson Comorbidity Index	0.88 ± 1.01	1.28 ± 1.34	0.24 <sup>a)</sup>

2 Data are expressed as mean ± SD

3 a) Student's t-test

4 b) Fisher's exact test

5 RAMIE, robot-assisted minimally invasive esophagectomy

6 UICC, the Union for International Cancer Control (8<sup>th</sup> Edition)

7 NAC / NACRT, neoadjuvant chemotherapy / neoadjuvant chemoradiotherapy

1 Table 2. Demographic and clinical characteristics of patients

	Early group (n = 6)	Late group (n = 19)	P
Age	66.2 ± 9.1	68.1 ± 10.4	0.678 <sup>a)</sup>
Gender			1.000 <sup>b)</sup>
Male / Female	3 (50%) / 3 (50%)	10 (53%) / 9 (47%)	
Height (cm)	165.3 ± 6.3	162.6 ± 9.4	0.52 <sup>a)</sup>
Weight (kg)	54.5 ± 2.6	58.4 ± 10.7	0.391 <sup>a)</sup>
Preoperative therapy			1.000 <sup>b)</sup>
NAC / NACRT / None	3 (50%) / 0 (0%) / 3 (50%)	10 (53%) / 0 (0%) / 9 (47%)	
RAMIE / Thoracoscopic / Mediastinoscopic	3 (50%) / 3 (50%) / 0 (0%)	16 (84%) / 2 (11%) / 1 (5%)	0.123 <sup>b)</sup>
UICC-cStage			0.055 <sup>b)</sup>
0	0	1 (5%)	
I	4 (66%)	2 (11%)	
II	0	5 (26%)	
III	1 (17%)	9 (47%)	
IV	1 (17%)	2 (11%)	
Charlson Comorbidity Index	0.50 ± 0.55	1.00 ± 1.11	0.302 <sup>a)</sup>

2 Data are expressed as mean ± SD

3 c) Student's t-test

4 d) Fisher's exact test

5 RAMIE, robot-assisted minimally invasive esophagectomy

6 UICC, the Union for International Cancer Control (8<sup>th</sup> Edition)

7 NAC / NACRT, neoadjuvant chemotherapy / neoadjuvant chemoradiotherapy

1 Table 3. Surgical outcomes (Early group vs Late group)

	Early group (n = 6)	Late group (n = 19)	P
Operative time (min)			
Overall procedure	694.5 [628.5–752.3]	798.0 [715.0–864.5]	0.031 <sup>c)</sup>
Retrosternal route creation	28.5 [18.3–39.5]	15.0 [13.0–19.0]	0.038 <sup>c)</sup>
Total blood loss (ml)	65.0 [20.0–80.0]	10.0 [10.0–51.5]	0.234 <sup>c)</sup>
Pleural injury			1.000 <sup>b)</sup>
Yes	1 (17%)	4 (21%)	
No	5 (83%)	15 (79%)	
Anastomotic leakage			0.606 <sup>b)</sup>
Yes	2 (33%)	4 (21%)	
No	4 (67%)	15 (79%)	
Other complications $\geq$ Grade II <sup>a)</sup>			1.000 <sup>b)</sup>
Yes	3 (50%)	9 (47%)	
No	3 (50%)	10 (53%)	
Histological type			1.000 <sup>b)</sup>
SqCC / Others	5 (83%) / 1 (17%)	16 (84%) / 3 (16%)	
Postoperative hospital stay	30.0 [24.0–48.0]	24.0 [22.0–29.0]	0.306 <sup>c)</sup>

2 Data are expressed as median and [25–75% interquartile range]

3 a) Grades are based on the Clavien–Dindo classification of surgical complications

4 b) Fisher's exact test

5 c) Wilcoxon rank-sum test

6 SqCC, squamous cell carcinoma

1 Table 4. Surgical outcomes (Retrosternal vs Posterior mediastinal)

	Retrosternal (n = 25)	Posterior mediastinal (n = 25)	P
Operative time (min)			
Overall procedure	782.0 [702.0–839.0]	677.0 [597.0–741.0]	0.008 <sup>c)</sup>
Total blood loss (ml)	10.0 [10.0–70.0]	30.0 [10.0–80.0]	0.5 <sup>c)</sup>
Anastomotic leakage			0.725 <sup>b)</sup>
Yes	6 (24%)	4 (16%)	
No	19 (76%)	21 (84%)	
Other complications $\geq$ Grade II <sup>a)</sup>			0.244 <sup>b)</sup>
Yes	12 (48%)	7 (28%)	
No	13 (52%)	18 (72%)	
Histological type			1.000 <sup>b)</sup>
SqCC / Others	21 (84%) / 4 (16%)	21 (84%) / 4 (16%)	
Postoperative hospital stay	26.0 [22.0–30.0]	22.0 [17.0–29.0]	0.066 <sup>c)</sup>
LA classification (one year after surgery)			0.32 <sup>c)</sup>
>A	1 (4%)	2 (8%)	
M	0 (0%)	2 (8%)	
N	12 (48%)	14 (56%)	
Not Available	12 (48%)	7 (28%)	
Conduit stenosis (one year after surgery)			0.26 <sup>c)</sup>
Yes	1 (4%)	3 (12%)	
No	12 (48%)	15 (60%)	
Not Available	12 (48%)	7 (28%)	

2 Data are expressed as median and [25–75% interquartile range]

3 a) Grades are based on the Clavien–Dindo classification of surgical complications

4 b) Fisher's exact test

- 1 c) Wilcoxon rank-sum test
- 2 SqCC, squamous cell carcinoma
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