Original Article

Short-term clinical effects of robot-assisted esophagectomy with thoracic duct resection

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Background: Whether extended robot-assisted esophagectomy with thoracic duct resection (RAE-TDR) has a favorable effect on esophageal cancer patients is not yet known. This study sought to analyze the safety and efficiency of RAE-TDR.

Methods: From January 2019 to July 2020, 73 thoracic duct (TD)-resected and 127 TD-preserved consecutive patients who received standard RAE McKeown surgery were enrolled in this study. The perioperative-related indicators of recurrence-free survival (RFS) and overall survival (OS) at 1-year were compared between the 2 groups.

Results: In relation to morbidity, the Clavien–Dindo (CD) classifications for grades greater than or equal to II–III were similar between the 2 groups (P>0.05). The number of retrieved total lymph nodes (LNs) and mediastinal nodes were significantly higher in the TD-resected group than in the TD-preserved group (total lymph nodes: 29.0±11.1 *vs.* 25.1±8.5, P=0.006; mediastinal nodes: 19.5±8.0 *vs.* 16.1±5.5, P=0.002). Additionally, more metastatic TD-related LNs were harvested in cT3–4 patients (2.3±3.7 *vs.* 1.7±2.8; P=0.21). The rates of LN recurrence and local recurrence were similar between the 2 groups (LN recurrence: 6.8% *vs.* 7.1%, P>0.99; local recurrence: 1.4% *vs.* 2.4%, P>0.99). The OS and RFS at 1-year were equivalent regardless of the TD procedure at each stage (P>0.05). However, the rate of hematogenous metastasis in the TD-resected group was significantly elevated (17.8% *vs.* 7.9%; P=0.034).

Conclusions: RAE-TDR may help to improve total and metastatic LN harvest, especially in patients with advanced esophageal squamous cell carcinoma (ESCC) without increasing the intra- and post-operative adverse events. However, RAE-TDR did not lead to a decrease in the local recurrence rate within the short-term follow-up period. Whether the increase in distant metastasis rate in the TD-resected group was associated with relevant immune system damage is unclear. Thus, nonselective RAE-TDR is not routinely recommended.

Keywords: Esophageal cancer; robot-assisted esophagectomy; thoracic duct (TD)

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Introduction

Despite multimodality treatment plans playing an increasingly important role in the treatment of patients with esophageal squamous cell carcinoma (ESCC), esophagectomy with lymph node (LN) dissection remains one of the most effective methods (1). However, a standard procedure to enhance the control of local recurrence and distal metastasis still needs to be defined. Additionally, the 5-year survival of patients with ESCC remains unsatisfactory due to the occurrence of LN metastasis at the early stage (2).

ESCC LN metastasis occurs both vertically and horizontally (3). Mediastinal thoracic duct lymph nodes (TDLNs) lie within the adipose and connective tissue between the descending aorta and azygos vein (4). A complete lymphadenectomy should include the resection of the thoracic duct (TD), TDLNs, and surrounding tissues. The incidence of TDLN metastasis is reported to be approximately 2–11% (5). Previous studies have revealed that thoracic duct resection (TDR) is associated with both reduced hematogenous and local recurrence in patients with more advanced ESCC; thus, TDR leads to improved clinical outcomes (6,7). However, this procedure has raised debates due to concerns about its perioperative complications, including higher intraoperative bleeding, more frequent Clavien–Dindo (CD) classifications for grade ≥ II complications, and pulmonary morbidities (8,9). To date, there has been limited research on whether TDR definitively improves patients' short- and long-term outcomes.

Robot-assisted minimally invasive esophagectomy (RAMIE) facilitates complex, minimally invasive surgical procedures and has multiple advantages, including an enlarged 3-dimensional (3D) view, 540° wrist articulation, and greater magnification (10,11). Furthermore, RAMIE offers precise dissection in the narrow working space in the posterior mediastinum, and is oncologically acceptable in terms of its shorter operating time, lower blood loss, and reduced pulmonary complications (12).

To our knowledge, no previous study has investigated the short- and long-term outcomes of robot-assisted esophagectomy with thoracic duct resection (RAE-TDR) for esophageal cancer. We prospectively analyzed a cohort of ESCC patients who underwent RAE and explored the effects of TDR on intra- and post-operative complications. We also examined recurrence-free survival (RFS) and overall survival (OS) at 1-year after surgery to evaluate the efficacy of RAE-TDR. We present the following article in accordance with the STROBE reporting checklist (available at https://jgo.amegroups.com/article/view/10.21037/jgo-22-985/rc).

Highlight box

Key findings

- RAE-TDR may help to improve total and metastatic LN harvest. However, RAE-TDR did not lead to a decrease in the local recurrence rate within the short-term follow-up period.

What is known and what is new?

- The question of whether TDR and surrounding LN dissection are necessary steps in esophageal cancer surgery has been controversial.
- No previous related study has investigated the short- and long-term outcomes of RAE-TDR for esophageal cancer. RAE-TDR did not lead to a decrease in the local recurrence rate within the short-term follow-up period.

What is the implication, and what should change now?

- Nonselective RAE-TDR is not routinely recommended for patients with esophageal cancer. To explore whether thoracic duct resection can improve the prognosis of patients is necessary in a prospective multicenter study.

Patients and methods

This single-center cohort study comprised 200 consecutive patients diagnosed with ESCC who received McKeown RAE at the Shanghai Chest Hospital between January 2019 and July 2020. Between 2019 and 2020, 127 consecutive ESCC patients received standard McKeown RAE surgery without TDR. From 2020 onward, esophagectomy with extended LN and TDR was executed in 73 patients. All participants were diagnosed preoperatively by endoscopy, enhanced contrast computed tomography (CT), and biopsy. Primarily resectable ESCC was defined as cT1–4a, N0–2, and M0 according to the staging system of the American Joint Committee for Cancer (seventh edition) (13). In our study, surgeons performing ≥40 RAE cases annually were considered sufficiently skilled, and RAE was completed with the help of the da Vinci surgical system. This study was approved by the Ethics Committee of Shanghai Chest Hospital (No. KS1734) and conducted in accordance with the Declaration of Helsinki (as revised in 2013). Informed consent was taken from all patients.

The standard esophagectomy conducted in our study was defined as a 3-incision McKeown surgery (left neck, left chest, and abdomen) with at least 2 fields of (thoracoabdominal) lymphadenectomy according to the Japanese Classification of Esophageal Cancer (14-16). The surgical procedures are described in our previous publication (17). Complete mesoesophageal resection involving TDR was performed as follows: after the azygos vein dissection, TD and the surrounding soft tissue, including the LNs, were dissected from the left mediastinum pleural surface to the esophageal side starting

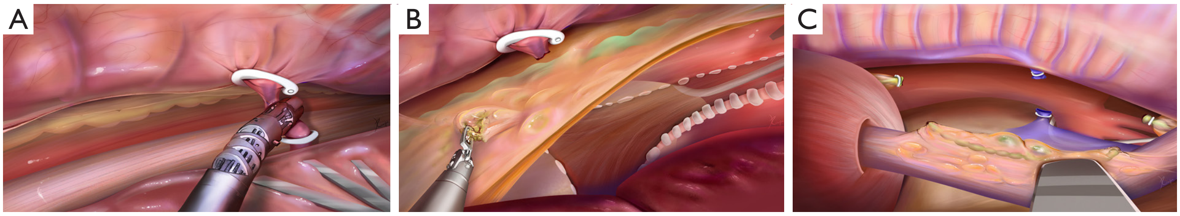

Figure 1 Schematic diagram of RAE-TDR. (A) The azygos arch was dissociated and severed; (B) the TD and surrounding soft tissue were removed; (C) the excision boundary ranged from the intersection of the TD with the left recurrent laryngeal nerve to the level of the 10th thoracic vertebra. RAE-TDR, robotic-assisted mesoesophagectomy with thoracic duct resection; TD, thoracic duct.

from the superior mediastinum. Continuing down to the descending aorta, the TD and surrounding soft tissue were completely removed, including the LNs, between the azygos vein and the aorta. The excision boundary ranged from the intersection of the TD with the left recurrent laryngeal nerve (RLN) to the level of the 10th thoracic vertebra. A schematic diagram of the robot-assisted mesoesophagectomy with TDR is shown in *Figure 1*. All patients were followed up in the outpatient clinic every 1 to 3 months. The follow-up visits were terminated following death or at 1-year after surgery.

Statistical analysis

The statistical analysis in our study was performed using SPSS 24.0 (IBM Corp., Armonk, NY, USA). The continuous variables were expressed as the mean ± standard deviation (M ± SD), and differences between the groups were analyzed using the Mann–Whitney *U* test or Student's *t*-test according to the homoscedasticity of variance. The categorical variables in different groups were assessed using the chi-squared test or Fisher's exact test. The survival curves were estimated using the Kaplan–Meier method, and the survival distribution was compared using the log-rank test. Statistical significance was considered when P≤0.05.

Results

Patient characteristics

A total of 200 ESCC patients underwent McKeown RAE with at least 2-field LN dissection at Shanghai Chest Hospital between January 2019 and July 2020. The TD-resected group comprised 73 patients and the TD-preserved group comprised 127 patients. The patient characteristics are presented in *Table 1*. The outcomes of the 2 groups were comparable in terms of the baseline characteristics, cTNM stage, pTNM stage, and preoperative therapy. The mean age of patients in the TD-resected group was 63.5±10.3 years, and that of the TD-preserved group was 65.9±7.5 years (P=0.056). The TD-resected group comprised 63 males and 10 females, whereas the TD-preserved group comprised 104 males and 23 females (P=0.418).

Anticancer treatment, including neoadjuvant chemotherapy, neoadjuvant chemoradiotherapy, neoadjuvant chemotherapy combined with immunotherapy, definitive chemoradiotherapy, and radiotherapy, was performed in 29 and 39 patients in the TD-resected and TD-preserved groups, respectively; however, there were no statistical differences between the 2 groups in terms of the preoperative treatment (P=0.195) or tumor regression status (P=0.096).

Intra- and post-operative parameters

The operative time for the thoracic phase (P=0.088) and total time (P=0.091) of RAE were calculated, and no significant differences were observed between the TD-resected group and TD-the preserved group. The bleeding volume of the TD-resected group was significantly lower than that of the TD-preserved group (P=0.008). In terms of complete resection, there were no differences in the distribution of the R0 resection status between the 2 groups (P=0.387). As *Table 2* shows, 63 patients (86.3%) and 113 patients (89.0%) underwent R0 resection in the TD-resected and TD-preserved groups, respectively. However, 9 patients (12.3%) in the TD-resected group and 14 patients (11.0%) in the TD-preserved group had a positive circumferential resection margin (R1 resection). Further, a residual tumor was confirmed in the tracheal membrane of 1 patient in the TD-resected group (R2 resection).

The postoperative comorbidities were also compared, but no significant differences were detected between the

Table 1 Demographic and clinical characteristics

Characteristics	TD-resected (n=73)	TD-preserved (n=127)	P value
Age, years, M ± SD	63.5±10.3	65.9±7.5	0.056
Gender, n (%)			0.418
Male	63 (86.3)	104 (81.9)	
Female	10 (13.7)	23 (18.1)	
BMI, n (%)			0.234
<18.5 kg/m^2	3 (4.1)	9 (7.1)	
18.5–24 kg/m^2	40 (54.8)	80 (63.0)	
>24 kg/m^2	30 (41.1)	38 (29.9)	
ASA score, n (%)			0.923
2	47 (64.4)	79 (62.2)	
3	26 (35.6)	47 (37.0)	
4	0	1 (0.8)	
Tumor location, n (%)			0.15
Upper	7 (9.6)	13 (10.2)	
Middle	40 (54.8)	52 (40.9)	
Lower	26 (35.6)	62 (48.8)	
cT stage, n (%)			0.287
T1	5 (6.8)	9 (7.1)	
T2	16 (21.9)	35 (27.6)	
T3	50 (68.5)	83 (65.4)	
T4	2 (2.7)	0	
cN stage, n (%)			0.135
N0	12 (16.4)	34 (26.8)	
N1	41 (56.2)	69 (54.3)	
N2	20 (27.4)	22 (17.3)	
N3	0	2 (1.6)	
cTNM stage, n (%)			0.103
I	4 (5.5)	9 (7.1)	
II	17 (23.3)	49 (38.6)	
III	50 (68.5)	67 (52.8)	
IVa	2 (2.7)	2 (1.6)	
pT stage, n (%)			0.852
T0	12 (16.4)	16 (12.6)	
T1	13 (17.8)	27 (21.3)	
T2	12 (16.4)	20 (15.7)	
T3	36 (49.3)	64 (50.4)	

Table 1 (*continued*)

Table 1 (*continued*)

Characteristics	TD-resected (n=73)	TD-preserved (n=127)	P value
pN stage, n (%)			0.304
N0	31 (42.5)	65 (51.2)	
N1	25 (34.2)	33 (26.0)	
N2	9 (12.3)	21 (16.5)	
N3	8 (11.0)	8 (6.3)	
pTNM stage, n (%)			0.348
I	19 (26.0)	32 (25.2)	
II	15 (20.5)	39 (30.7)	
III	31 (42.5)	48 (37.8)	
IVa	8 (11.0)	8 (6.3)	

TD, thoracic duct; M ± SD, mean ± standard deviation; BMI, body mass index; ASA, American Society of Anesthesiologists.

Table 2 Intra- and postoperative parameters

Parameters	TD-resected	TD-preserved	P value
Intraoperative			
Duration of operation (min), M ± SD			
Total	283.2±55.9	262.1±46.8	0.091
Thoracic phase	98.0±21.5	93.1±18.2	0.088
Bleeding (mL), M ± SD	139.0±48.8	160.6±57.9	0.008*
Resection status, n			0.387
R0	63	113	
R1	9	12	
R2	1	2	
Postoperative			
CD grade > II, n	11	17	0.741
CD grade > III, n	8	8	0.242
Pneumonia, n	8	8	0.242
Chylothorax, n	6	6	0.361
RLN palsy, n	12	28	0.342
Anastomotic leakage, n	2	5	1.0
Duration of drainage (day), M ± SD	4.4±2.7	4.4±3.2	0.999
Length of ICU stay (day), M ± SD	1.5±1.4	1.4±1.7	0.643
Length of hospital stay (day), M ± SD	9.5±4.5	9.6±4.3	0.882

*P<0.05. TD, thoracic duct; M ± SD, mean ± standard deviation; CD, Clavien-Dindo; RLN, recurrent laryngeal nerve; ICU, intensive care unit.

Table 3 Number of dissected LNs according to TD status

Location of lymph nodes	TD-resected	TD-preserved	P value
Total LNs	29.0±11.1	25.1±8.5	0.006*
Cervical	2.9±4.4	1.9±3.8	0.119
Thoracic	19.5±8.0	16.1±5.5	0.002*
Abdominal	6.6±4.1	7.0±3.7	0.394
Total positive LNs	2.3±3.7	1.7±2.8	0.210
Cervical	0.2±0.6	0.1±0.6	0.659
Thoracic	1.3±2.3	1.0±1.9	0.350
Abdominal	0.9±1.9	0.6±1.3	0.164

*P<0.05. Data are presented as mean ± standard deviation. LN, lymph node; TD, thoracic duct.

2 groups (P=0.432). Notably, 23 (31.5%) and 47 (37.0%) patients in the TD-resected and TD-preserved groups, respectively, experienced at least 1 complication after surgery. The rates of CD stage II–III complications, including chylothorax (P=0.36), left RLN palsy (P=0.34), and anastomotic leakage (P=1.0), were comparable between the 2 groups. Pulmonary complications occurred in 8 TD-resected and 8 TD-preserved patients (P=0.242). The thoracic drainage times were 4.4±2.7 days in the TD-resected group and 4.4±3.2 days in the TD-preserved group, and there was no difference between the 2 groups (P=0.999). The lengths of postoperative intensive care unit (ICU) and hospital stays in the TD-resected patients were 1.5±1.4 days and 9.5±4.5 days, respectively, and did not differ significantly to those of the TD-preserved patients whose ICU and hospital stays were 1.4±1.7 days (P=0.643) and 9.6±4.3 days (P=0.882), respectively.

The number of total retrieved nodes and mediastinal nodes were significantly higher in the TD-resected group than in the TD-preserved group (P=0.006 and P=0.002, respectively). As for the number of tumor-infiltrated LNs, there were no differences between the 2 groups irrespective of the operation phase (see *Table 3*). However, 8 patients (11%) in the TD-resected group had metastatic TD LNs. We also compared the number of total and metastatic mediastinal LNs according to cT stage and found that more mediastinal LNs were retrieved (P<0.001) in the TD-resected group than in the TD-preserved group (see *Table 4*), especially No. 109R (P=0.006), No. 110 (P=0.049), and No. 111 (P<0.001) LNs; however, there were no significant differences in the metastatic mediastinal LNs between the 2 groups. We compared the metastatic and total mediastinal LNs in cT stage 3/4 tumors, and found that more mediastinal LNs were harvested in the TD-resected group than in the TD-preserved group (P<0.001; see *Table 5*). In the TD-resected group, 2 (9.50%) and 6 (11.53%) patients had metastatic TDLNs in cT stage 1–2 and cT stage 3–4, respectively (P>0.05).

Relationship between TDR and short-term outcomes

Across all stages, the OS at 1 year after surgery of the TD-resected group (94.52%) was higher than that of the TD-preserved group (90.55%); however, the survival curves did not differ significantly (P=0.402, log-rank test; see *Figure 2A*). Additionally, the RFS at 1 year of the TD-resected patients (76.71%) was lower than that of the TD-preserved patients (85.04%), with the curves being similar (P=0.996; see *Figure 2B*).

We further analyzed the 1-year OS and RFS according to the clinical stages. The 1-year OS of the stage I–II and stage III–IV patients were similar regardless of the TDR status (P=0.953 and P=0.317) (see *Figure 2C,2D*). Additionally, 1-year RFS was found to be irrelevant to TDR status in stage I–II (P=0.976) and stage III–IV (P=0.903) patients (see *Figure 2E,2F*).

The postoperative recurrence patterns are shown in *Table 6*. The incidence of hematogenous recurrence at 1 year after surgery was significantly lower in the TD-preserved group (7.9%) than in the TD-resected group (17.8%; P=0.034). However, the liver, bone, lung, brain, and other hematogenous metastases were similar in the 2 groups. The incidences of LN recurrence (P>0.99) and local recurrence (P>0.99) during the 1-year follow-up did

Table 4 Number of total and metastatic mediastinal LNs in all stages

Location of lymph nodes	Metastatic			Total		
	TD-resected	TD-preserved	P value	TD-resected	TD-preserved	P value
105	0.05±0.23	0.06±0.30	0.84	1.16±1.43	1.23±1.57	0.78
106R	0.44±0.96	0.38±0.98	0.67	2.59±2.23	2.79±1.91	0.51
106L	0.12±0.55	0.14±0.45	0.80	2.37±1.94	2.08±1.78	0.28
107	0.11±0.42	0.06±0.26	0.26	2.59±1.90	3.12±2.13	0.08
108	0.07±0.30	0.09±0.41	0.64	2.03±1.80	1.61±1.62	0.10
109R	0.05±0.23	0.02±0.12	0.12	1.86±1.78	1.20±1.54	0.006*
109L	0.03±0.16	0.08±0.35	0.24	1.73±1.94	1.54±1.86	0.50
110	0.19±0.61	0.12±0.37	0.29	1.71±1.61	1.26±1.52	0.049*
111	0.05±0.23	0.05±0.25	0.83	0.96±0.97	0.42±0.74	<0.001*
TDLN	0.15±0.49	NA		1.59±1.83	NA	
Total	1.27±2.30	0.99±1.85	0.35	18.59±7.52	15.24±5.18	<0.001*

*P<0.05. Data are presented as mean ± standard deviation. TD, thoracic duct; TDLN, thoracic duct lymph node; NA, not available.

Table 5 Number of total and metastatic mediastinal LNs in cT3–4 stage

Location of lymph nodes	Metastatic			Total		
	TD-resected	TD-preserved	P value	TD-resected	TD-preserved	P value
105	0.06±0.24	0.09±0.37	0.58	1.31±1.62	1.21±1.68	0.66
106R	0.51±1.05	0.51±1.19	0.61	2.45±1.74	2.84±1.79	0.52
106L	0.16±0.65	0.19±0.53	0.59	2.16±1.66	2.01±1.69	0.72
107	0.14±0.49	0.07±0.30	0.62	2.51±1.96	3.28±2.29	0.40
108	0.10±0.36	0.11±0.45	0.59	2.02±1.77	1.48±1.55	0.86
109R	0.06±0.24	0.01±0.11	0.61	1.49±1.42	1.33±1.70	0.69
109L	0.02±0.14	0.11±0.42	0.56	1.24±1.39	1.49±1.96	0.54
110	0.24±0.69	0.15±0.42	0.63	1.67±1.67	1.24±1.52	0.81
111	0.06±0.24	0.08±0.32	0.59	0.84±0.98	0.40±0.75	0.77
TDLN	0.20±0.57	NA		1.69±1.86	NA	
Total	1.57±2.58	1.31±2.12	0.74	17.39±6.01	15.29±5.44	0.022*

*P<0.05. Data are presented as mean ± standard deviation. TD, thoracic duct; TDLN, thoracic duct lymph node; NA, not available.

not differ between the 2 groups.

Discussion

The question of whether TDR and surrounding LN dissection are necessary steps in esophageal cancer surgery has been controversial. Concerns arise as to whether this approach increases surgical complications, whether it can control local recurrence, and whether it will lead to long-term harm due to its effects on humoral immune circulation. Thus, we sought to examine the use of RAE-TDR in homogenous, high-precision robotic surgery in which the learning curve had been completed.

Chylothorax and RLN palsy are the 2 most common

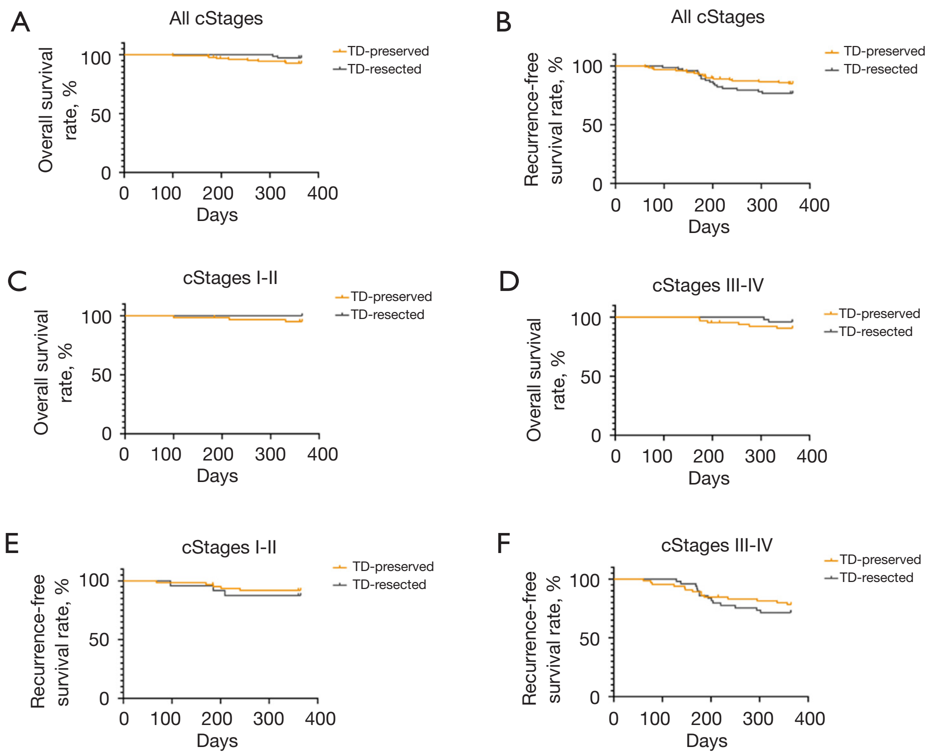

Figure 2 Relationship between TDR and survival results. (A) All stages: the OS at 1 year after surgery of the TD-resected group (94.52%) was higher than that of the TD-preserved group (90.55%); however, the survival curves did not differ significantly (P=0.402; log-rank). (B) The RFS at 1 year of the TD-resected patients (76.71%) was lower than that of the TD-preserved patients (85.04%), with the curves being similar (P=0.996). (C) The 1-year OS in stage I–II patients were similar regardless of TDR status (P=0.953). (D) The 1-year OS in stage III–IV patients was similar regardless of TDR status (P=0.317). (E) The 1-year RFS was found to be irrelevant to TDR status in stage I–II (P=0.976) patients. (F) The 1-year RFS was found to be irrelevant to TDR status in stage III–IV patients (P=0.903). TDR, thoracic duct resection; OS, overall survival; RFS, recurrence-free survival.

Table 6 Initial recurrence patterns

Location	TD-resected (n=73), n (%)	TD-preserved (n=127), n (%)	P value
Hematogenous metastasis	13 (17.8)	10 (7.9)	0.034*
Liver	2 (2.7)	4 (3.1)	>0.99
Bone	4 (5.4)	3 (2.4)	0.261
Lung	4 (5.4)	4 (3.1)	0.467
Brain	2 (2.7)	1 (0.8)	0.555
Other	6 (8.1)	3 (2.4)	0.076
LN recurrence	5 (6.8)	9 (7.1)	>0.99
Local	3 (4.1)	3 (2.4)	0.670
Distant	5 (6.8)	6 (4.8)	0.534
Local recurrence	1 (1.4)	3 (2.4)	>0.99

*P<0.05. TD, thoracic duct; LN, lymph node.

complications after esophagectomy and are regarded as collateral damage to lymphadenectomy. RAE for esophageal cancer has been increasingly performed at several large international reference centers. The minimally invasive effect and higher efficacy of regional LN dissection have been demonstrated (10,17). Under the robot-assisted system, better visualization and a flexible but steady robot arm allows the surgeon to precisely and completely dissect the TD, TDLNs, LNs, and RLN without any other accidental injuries.

In our study, the number of dissected LNs in the thorax was significantly increased by TDR, which is consistent with previous reports (12,17). We also discovered that the number of dissected LNs in stations 109R, 110, and 111 was significantly higher in the TD-resected group than in the TD-preserved group. Despite of the insignificant statistical power, more metastatic mediastinal LNs, including positive TDLNs, were harvested in the TD-resected patients, which may have a favorable effect in preventing tumor metastasis.

There is still considerable debate about the long-term survival effects of TDR. The only possible positive effects of TDR are to achieve greater LN dissection and avoid the presence of occult metastatic LNs. The spatial relationship of the TD and its surrounding LNs is very difficult to define, especially if the TD is in close proximity to the middle and upper paraoesophageal LNs. In relation to LN metastasis in esophageal cancer, if the invasion is above T2, the metastatic LNs will significantly metastasize to the tumor side wall and have the potential to drain directly into the TD. Complete TDR is thus beneficial to obtaining the effect of a radical *en bloc* tumor resection. The complete resection of TD should include the TD, TDLNs, and adipose tissues surrounding the TD, as the incidence of TDLN metastasis has been reported to be approximately 2–11%, and some patients with ESCC have been reported to have TDLN recurrence after radical esophagectomy; thus, it has been proposed that joint resection with TDR may improve the long-term outcomes of patients (5).

Tanaka *et al.* conducted a retrospective, multi-institutional analysis in which they compared the outcomes of 2,269 patients receiving esophagectomy with and without TDR and concluded that TDR is associated with both reduced hematogenous and local recurrence in local advanced ESCC patients and thus leads to improved short- and long-term outcomes (6). However, some studies have found that TDR produces survival benefits even in T1 patients (7,18). This appears to contradict the previous rule of LN metastasis that states that LNs will metastasize up and down the submucosa and form lesions beside the recurrent laryngeal nerve and around the cardia in T1 patients.

In addition to greater tumor resection, TDR and its surrounding LN dissection may also have negative effects. In Matsuda *et al.*'s study, the TD-preserved group had a more favorable RFS curve than did the TD-resected group among patients who underwent esophagectomy for c-stage II–IV ESCC (18). Additionally, Hou *et al.* a conducted a multivariate Cox regression analysis and reported that TD ligation during esophagectomy unfavorably affected the OS of patients with esophageal cancer (19). Recently, a large-scale multicenter cohort study Japan suggested that TD resection can obtain more positive LNs, but it may lead to worse long-term survival and more distant organ metastasis. Our findings were consistent with this (20).

As an independent human organ, the TD should be protected. The TD is indispensable in immune function and nutrition circulation, as it is the largest lymphatic vessel and drains about 75% of the lymph, with rich ingested fats, proteins, T lymphocytes, and various immune components; thus, the ligation or resection of the TD may result in hemodynamic disturbances and malnutrition (21,22). The TD also lets intestinal chyle flow into the venous system, and the continued interruption of chyle flow can lead to immunosuppression and impaired B-lymphocyte–mediated immune function, which may worsen the outcomes of TD-resected patients (23). T follicular helper (Tfh) cells in germinal centers of secondary lymphoid organs are pivotal for humoral immunity. Circulating Tfh cells can inhibit micrometastasis of tumors. The TD is the main route of Tfh cell traffic from lymphatic system to blood system (24). Therefore, after thoracic duct resection, humoral immunity is impaired which may lead to more distant organ metastasis.

In our study, the intra- and post-operative parameters were almost comparable between the 2 groups except that the bleeding volume was lower in the TD-resected group. The 1-year OS, RFS, and recurrence patterns across all stages were similar among the TD-resected and TD-preserved patients. This is mainly due to the short follow-up time. However, the distant metastasis rate of the TD-resected group was much higher than that of TD-preserved group. This may have been due to immune system damage after TDR. Thus, it appears that TDR and peripheral LN dissection should be performed in patients with a high risk of LN metastasis to minimize the risk of surgery.

Our study had some limitations, including its small volume of samples and its recruitment of participants from only 1 center. Additionally, propensity score matching was not performed to minimize selection bias before the analysis, as the baseline characteristics were considered comparable. Finally, the follow-up period was too short to reach a significant end point.

In conclusion, the technique of RAE-TDR is safe, does not increase postoperative complications, and only slightly prolongs the operation time. RAE-TDR may help to improve the total and metastatic harvest of LNs, especially in patients with advanced ESCC, without increasing the intra- and postoperative incidence of adverse events. However, RAE-TDR does not lead to a decrease in the local recurrence rate in the short-term. Whether the increase in distant metastasis rate in the TD-resected group was associated with relevant immune system damage is unclear. Thus, nonselective RAE-TDR is not routinely recommended.

Conclusions

RAE-TDR may help to improve total and metastatic LN harvest, especially in patients with advanced ESCC without increasing the intra- and post-operative adverse events. However, RAE-TDR did not lead to a decrease in the local recurrence rate within the short-term follow-up period. Thus, nonselective RAE-TDR is not routinely recommended.

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Footnote

Reporting Checklist: The authors have completed the STROBE reporting checklist. Available at https://jgo.amegroups.com/article/view/10.21037/jgo-22-985/rc

Data Sharing Statement: Available at https://jgo.amegroups.com/article/view/10.21037/jgo-22-985/dss

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Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://jgo.amegroups.com/article/view/10.21037/jgo-22-985/coif). All authors report that the study was supported by 2020 Shanghai "Rising Stars of Medical Talents" Youth Development Program to CGL, and the Shanghai Esophageal Cancer Cohort Database of Shanghai Hospital Development Center (No. SHDC2020CR6002) to ZGL. The authors have no other conflicts of interest to declare.

*Ethical Statemen*t: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. This study was approved by the Ethics Committee of Shanghai Chest Hospital (No. KS1734) and conducted in accordance with the Declaration of Helsinki (as revised in 2013). Informed consent was taken from all patients.

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Supplementary

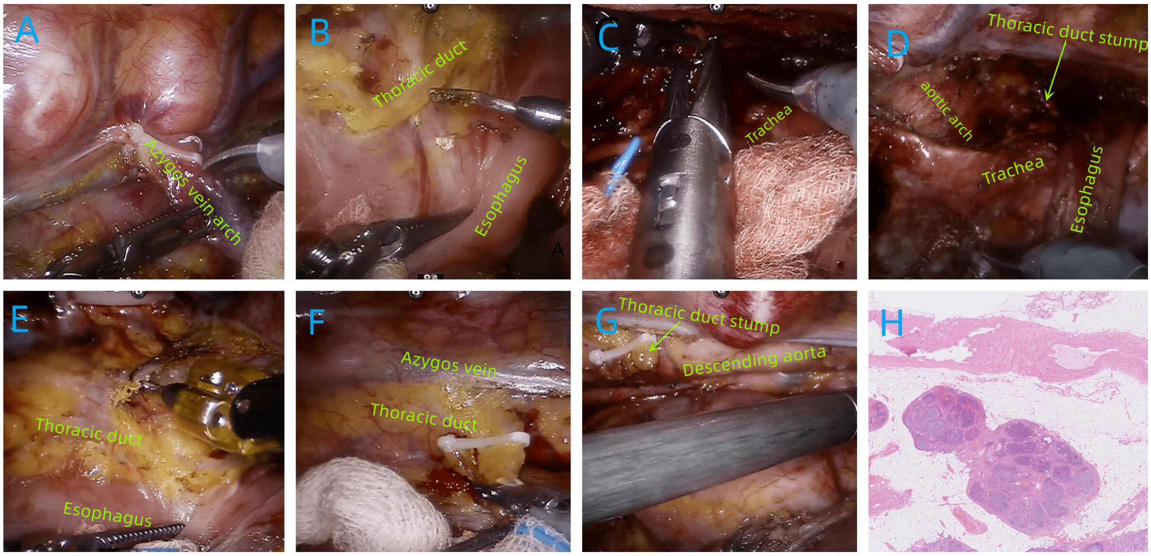

Figure S1 Steps of robotic assisted mesoesophagectomy with thoracic duct resection in the operation and pathologic images of positive thoracic duct lymph nodes. (A) The azygos arch was dissociated and severed; (B) the superior mediastinum thoracic duct and its surrounding soft tissue were removed; (C) the thoracic duct should be severed at the junction of the thoracic duct and the left recurrent laryngeal nerve; (D) this was a display of the upper mediastinum after thoracic duct resection; (E) the thoracic duct and its surrounding soft tissue below the level of azygos venous arch was dissociated and resected; (F) we divided the thoracic duct at the level of about the tenth thoracic vertebra; (G) this was a view of the inferior mediastinal after thoracic duct resection; (H) this was a pathologic view of thoracic duct lymph node with tumor metastasis. Tissue specimen was stained by hematoxylin-eosin. Primary magnification: ×200.

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