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Short- and long-term outcomes for early large esophageal carcinoma patients treated via double- and single-tunnel super minimally invasive surgery: a multicentre, retrospective cohort study

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Background and study aim Super minimally invasive surgery (SMIS) via endoscopic submucosal tunnel dissection (ESTD) has shown promising preliminary efficacy for the treatment of large early esophageal cancer (EEC). This study reports the short- and long-term outcomes of both single- and double-tunnel ESTD for large EEC.

Patients and methods All 90 patients with large EEC underwent ESTD at three hospitals between December 2013 and March 2024. We divided patients into two groups (single-tunnel SMIS and double-tunnel SMIS). Main outcome measurements: rates of en bloc resection, complete resection (R0 resection), curative resection, dissection speed and complications were evaluated as short-term outcomes. Overall survival, local or distant recurrence, and postoperative stricture rates were evaluated as long-term outcomes.

Results For all patients, the en bloc and R0 resection rates were 97.8% and 67.8%, respectively. Post-ESTD bleeding and fever were detected in 8.9% and 17.8% of the procedures, respectively. Postoperative stenosis and recurrence occurred in 54 patients (60.0%) and 7 patients (9.5%), respectively. Among the 90 patients with different circumferential-extent lesions, those who received a double-tunnel ESTD procedure (n = 54) underwent dissection faster than those who received a single-tunnel ESTD procedure (n = 36, 0.25 vs. 0.19 cm^2/min, $P = 0.012$). No statistically significant differences were observed between the two groups in terms of short-term postoperative complications, postoperative esophageal stenosis, survival or recurrence rates ($P > 0.05$). Multivariate regression analysis revealed that whole-circumferential lesions were an independent risk factor for technical difficulties.

Conclusion ESTD was effective for treating large early esophageal carcinoma. Compared with single-tunnel ESTD, double-tunnel ESTD has a faster resection speed, and there was no significant difference in short-term postoperative complications or long-term follow-up results. Therefore, double-tunnel ESTD is safe, reliable and more efficient in the treatment of large EEC.

Keywords Early esophageal carcinoma · Super minimally invasive surgery · Endoscopic submucosal tunnel dissection · Therapeutic efficiency · Short-term outcomes · Long-term outcomes

Superficial early esophageal carcinoma (EEC) can be cured by super minimally invasive surgery, SMIS [1, 2]. SMIS is

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defined as a surgical method that involves curing the disease while preserving organ function, which is different from traditional esophagectomy [1, 2]. SMIS for EEC typically includes the surgical methods of endoscopic submucosal dissection (ESD), endoscopic submucosal tunnel dissection (ESTD) and endoscopic mucosal resection, EMR [1, 2]. Currently, SMIS is the optimal choice for EEC patients with a low risk of lymph node metastasis (LNM). Patients have a greater quality of life because of complete organ preservation. For the treatment of large superficial EEC, ESTD seems to be a better choice due to its advantages of a shorter operative time, quick stripping speed, fewer complications, and high tumour resection rate [3, 4]. Since 2013, our centre has reported on this type of ESTD surgery, and this technique has been widely applied [5]. Our previous article reported the therapeutic effectiveness of single-tunnel and double-tunnel ESTD for large EEC between October 2011 and March 2016 [6]. One or two tunnels are created between the mucosa and muscularis propria, and the submucosal tunnels improve the endoscopic view to facilitate endoscopic dissection of lesions [5, 6]. However, most of the relevant data are limited to small-scale, single-centre clinical or short-term outcome studies. Therefore, a multicentre retrospective cohort study was conducted to continue our previous research and obtain data on the short- and long-term effects of improved single and double ESTD for large EEC.

Patients and methods

Patients

From December 2013 to March 2024, 90 patients diagnosed with EEC underwent ESTD at 3 hospitals in China (Chinese PLA General Hospital, Beijing; Drum Tower Hospital Affiliated with the Medical School of Nanjing University, Nanjing; Sichuan Cancer Hospital, Chengdu). All patients signed informed consent forms before ESTD surgery. This trial was approved by the Ethics Committee of Chinese PLA General Hospital (ethical approval number S2023-188-01).

The inclusion criteria were as follows: (1) single esophageal lesion with an endoscopic or pathological diagnosis of high-grade intraepithelial neoplasia (HGIN) or squamous cell carcinoma; (2) no lymph node or distant metastasis as indicated by enhanced CT or PET–CT; and (3) esophageal neoplastic lesions involving at least half of the esophageal circumference. The exclusion criteria were as follows: (1) history of other tumours; (2) history of organ resection surgery for gastrointestinal tumours; (3) serious cardiovascular, pulmonary, or hepatorenal diseases; and (4) other contraindications to endoscopic procedures and therapies.

SMIS via the ESTD procedure

As described previously [5, 6], the equipment and accessories included a single-accessory channel endoscope (GIFQ260J; Olympus, Tokyo, Japan), a transparent cap (D201-11804; Olympus), a triangle-tip knife (KD-640 L; Olympus), a dual knife (KD-650Q; Olympus), haemostatic forceps (FD-410LR; Olympus), an endoscopic injection needle (NM400L0425; Olympus), CO_2 insufflation, and a mixture of normal saline with 0.1% methylene blue and 0.5% epinephrine. The patient was in the left decubitus position and was administered intravenous propofol combined with anaesthesia.

The procedures were as follows (Fig. 1): (1) the lesion was marked, (2) the distal end of the mucosa was resected, (3) the proximal end of the mucosa was resected, (4) one or two tunnels were created, (5) the submucosa from the proximal to the distal end was separated, (6) the lateral mucosa was resected, and (7) haemostasis was achieved. In the double-tunnel ESTD, the width of each tunnel is approximately 1.5 cm.

Specimen and pathological calculation methods

The calculation standards for the sample area (cm^2), operative time (min), and dissection speed (cm^2/min) were the same as those in previous studies [6]. The T stage of EEC is based on the pathological type and infiltration depth of the tumour. The T stage includes high-grade intraepithelial neoplasia (HGIN) and squamous cell carcinoma (SCC), which are located in the mucosal epithelial layer. T1a includes SCCs invading the lamina propria and muscularis mucosae. T1b includes SCCs invading the submucosa [7].

Short-term outcomes

The rates of en bloc resection (defined as an entire sample without any fragmentation), R0 resection (defined as a disease-free resection margin), curative resection (defined as R0 resection with a depth of EEC invading SM1), dissection speed and complications were evaluated as short-term outcomes [6, 8]. The dissection speed (cm^2/min) was defined as the specimen area (cm^2) divided by the operative time (min). The short-term complications included muscular damage, cardiac mucosal laceration, perforation, post-ESTD bleeding, and postoperative fever (temperature > 38.1 °C) [8].

Postoperative management

In our study, preventive measures for post-ESTD stenosis included peroral steroid treatment (prednisolone at 30 mg/

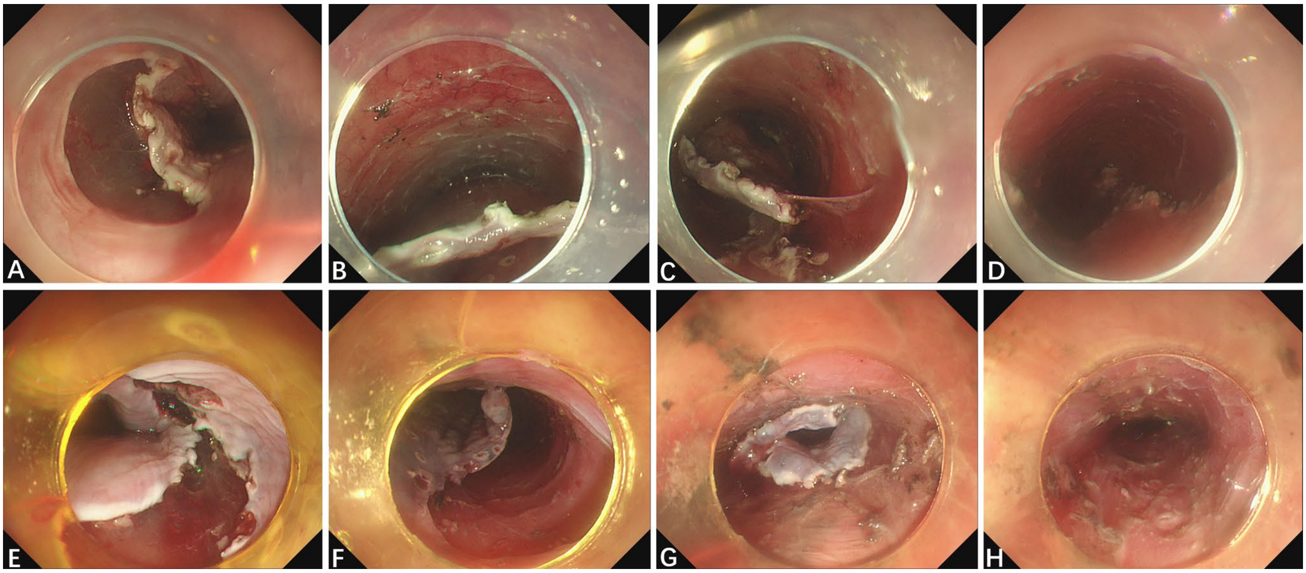

Fig. 1 **A**–**D** The procedures of single-tunnel ESTD. **E**–**H** The procedures of double-tunnel ESTD

day, followed by a weekly reduction of 5 mg), steroid injection [triamcinolone acetonide 0.5 ml (40 mg/ml) at 1-cm intervals for a total of 2 ml per injection], endoscopic balloon dilation (EBD, an average of 6 sessions required), prophylactic esophageal stent placement (8 to 12 weeks), autologous skin-grafting surgery, and EBD combined with steroids [9, 10].

EEC with no curative resection includes any lesion invading deeper than SM1 or any lesion with a positive vertical or horizontal margin or lymph or vascular invasion. Additional radiotherapy or surgical treatment is needed as supplementary treatment [10, 11]. Patients who refused supplementary treatment were advised to undergo close clinical follow-up.

Long-term outcomes

Postoperative stricture rates, overall survival (OS), disease-specific survival (DSS), and recurrence-free survival (RFS) were evaluated as long-term outcomes. Esophageal stenosis refers to the inability of ordinary endoscopy to pass through the esophagus during follow-up examination. The rates of OS, DSS and RFS were assessed through follow-up.

Statistical analysis

SPSS 29.0 software was used for data analysis. When describing data, metric data that follow a normal distribution are described using the mean ± standard deviation; nonnormally distributed econometric data are described using the median and interquartile range. When statistical analysis is conducted, quantitative indicators that follow a normal distribution are compared via two independent sample t tests, and the Z test is used for quantitative indicators with a nonnormal distribution. Qualitative data were analysed via the χ^2 test. A P value less than 0.05 indicated a significant difference.

Results

Clinical characteristics and endoscopic features

We enrolled 90 patients, including 62 males and 28 females aged 42–83 (average 63.06 ± 8.87) years. Thirty-six of the patients successfully received single-tunnel ESTD, and 54 received double-tunnel ESTD. Each patient had one lesion in their esophagus involving at least 1/2 of the esophageal circumference. A circumferential extent of ($\geq 1/2, < 3/4$) was identified in 12 lesions, ($\geq 3/4, < 1$) in 25 lesions, and ($= 1$) in 53 lesions. Among the 90 lesions, 9 were found to be located in the upper esophagus, 49 were located in the middle esophagus, and 32 were located in the lower esophagus. The macroscopic type was consistent with the Paris classification type 0–IIa, 0–IIb, or 0–IIc, or a combination of these [12, 13]. Among the 90 esophageal lesions studied, 27 (30.0%) were type 0–IIa, 49 (54.4%) were 0–IIb, 3 (3.3%) were 0–IIc, and the other 11 (12.2%) were mixed type. As shown in Table 1, there was a significant difference in the degree of circumferential lesions between the two groups ($P < 0.01$). For whole-circumferential lesions, double-tunnel ESTD treatment was mainly adopted, whereas for noncircumferential lesions, single-tunnel ESTD treatment was the preferred approach. In terms of other clinical and endoscopic characteristics (such as age, sex, lesion location,

Table 1 Clinical characteristics and endoscopic features

Items	Single-tunnel ESTD (n = 36)	Double-tunnel ESTD (n = 54)	P value	Total (n = 90)
Patients				
Age, mean ± SD (years)	64.39 ± 9.40	62.17 ± 8.48	0.247	63.06 ± 8.87
Gender, n (%)			0.926	
Male	25 (69.4%)	37 (68.5%)		62 (68.9%)
Female	11 (30.6%)	17 (31.5%)		28 (31.1%)
Lesion features				
Circumferential-extent, n (%)			< 0.001	
≥ 1/2, < 3/4	10 (27.8%)	2 (3.7%)		12 (13.3%)
≥ 3/4, < 1	19 (52.8%)	6 (11.1%)		25 (27.8%)
= 1	7 (19.4%)	46 (85.2%)		53 (58.9%)
Location, n (%)			0.380	
Upper	2 (5.5%)	7 (13.0%)		9 (10.0%)
Middle	19 (52.8%)	30 (55.6%)		49 (54.4%)
Lower	15 (41.7%)	17 (31.4%)		32 (35.6%)
Macroscopic type, n (%)			0.411	
0–IIa	13 (36.1%)	14 (25.9%)		27 (30.0%)
0–IIb	16 (44.4%)	33 (61.1%)		49 (54.4%)
0–IIc	2 (5.6%)	1 (1.9%)		3 (3.3%)
Mixed type	5 (13.9%)	6 (11.1%)		11 (12.2%)

and macroscopic classification), there was no statistically significant difference between the two groups (P > 0.05).

Short-term outcomes

Final pathological diagnosis

A final pathological analysis revealed that 19 samples (21.1%) were finally diagnosed as high-grade intraepithelial neoplasia (HGIN), and 71 samples (78.9%) were finally diagnosed as squamous cell carcinoma (SCC). The T stage distribution among the patients is as follows: Tis (17.8%), T1a (53.3%), and T1b (28.9%). Horizontal margin involvement and vertical margin involvement were identified in 20 lesions (22.2%) and 8 lesions (8.9%), respectively. Lymphovascular invasion was identified in 4 lesions (4.4%). As shown in Table 2, there was no statistically significant difference between the single- and double-tunnel groups in terms of pathology, such as type, stage and local infiltration (P > 0.05).

Procedure-related parameters

Each patient had one lesion in the esophagus. All patients had completed ESTD surgery. The rates of en bloc resection, R0 resection and curative resection were 97.8%, 70.0% and 58.9%, respectively. There were 41 patients with lesion areas ≤ 20 cm^2, and the remaining 49 patients had lesion

Table 2 Final pathological diagnosis

Pathological type	Single-tunnel ESTD (n = 36)	Double-tunnel ESTD (n = 54)	P value	Total (n = 90)
Pathological type, n (%)			0.752	
HGIN	7 (19.4%)	12 (22.2%)		19 (21.1%)
SCC	29 (80.6%)	42 (77.8%)		71 (78.9%)
T stage, n (%)			0.727	
Tis	6 (16.7%)	10 (18.5%)		16 (17.8%)
T1a	21 (58.3%)	27 (50.0%)		48 (53.3%)
T1b	9 (25.0%)	17 (31.5%)		26 (28.9%)
Horizontal margin involvement, n (%)	7 (19.4%)	13 (24.1%)	0.605	20 (22.2%)
Vertical margin involvement, n (%)	2 (5.6%)	6 (11.1%)	0.597	8 (8.9%)
Lymphovascular invasion, n (%)	0 (0.0%)	4 (7.4%)	0.251	4 (4.4%)

areas > 20 cm^2. The maximum long diameter of the seven samples was ≤ 4 cm, and those of the remaining samples were > 4 cm. The median operative time of the total sample was 100.50 (74.75–141.75) min, and the median resection speed was 0.23 (0.17–0.31) cm^2/min. In terms of short-term postoperative complications, 8 patients (8.9%) experienced postoperative bleeding, and 16 patients (17.8%) experienced postoperative fever. There were no adverse events, such as perforation, cardiac mucosal laceration, or muscular damage. As shown in Table 3, the en bloc resection rate of the double-tunnel group was greater than that of the single-tunnel group, but the difference was not statistically significant (100% vs. 94.4%, P = 0.307). In terms of the R0 and curative resection rates, those of the single-tunnel group were greater than those of the double-tunnel group, but the difference was also not statistically significant (69.4% vs. 66.7%, P = 0.782; 63.9% vs. 51.9%, P = 0.259). There were significant differences in the area and maximum long diameter of the resected samples between the two groups. The overall lesion area of the double-tunnel group was significantly larger than that of the other groups, and the long diameter was significantly greater (P = 0.004, 0.03). However, there was no significant difference in operative time between the two groups [99.50 (70.75–139.50) min vs. 103.00 (79.75–147.75) min, P = 0.422]. After calculation and analysis, there was a statistically significant difference in the lesion resection speed between the two groups, with the double-tunnel group having a significantly faster resection speed than the single-tunnel group [0.25 (0.19–0.36) cm^2/min vs. 0.19 (0.13–0.27) cm^2/min, P = 0.012]. In terms of short-term postoperative complications, there was no statistically significant difference in incidence between the two groups (P > 0.05).

Risk factors for technical difficulties

Technical difficulties were defined as the incidence of horizontal margin involvement, post-ESTD bleeding, muscular damage, and post-ESTD fever, which were 22.2% (20/90), 8.9% (8/90), 0.0% (0/90), and 17.8% (16/90), respectively. The number of events includes all events above. Among the patients with technical difficulties, each was found to experience one or more events (Fig. 2). Therefore, by analysing clinical data, the technical difficulty rate was calculated to be 40% (36/90) in the present study. All patients with adverse events were successfully treated with endoscopic therapy or conservative treatment.

Understanding the risk factors for the technical difficulty of esophageal ESTD could help endoscopists accurately

Table 3 Procedure-related parameters

Items	Single-tunnel ESTD (n = 36)	Double-tunnel ESTD (n = 54)	P value	Total (n = 90)
En bloc resection, n (%)			0.307	
Yes	34 (94.4%)	54 (100.0%)		88 (97.8%)
No	2 (5.6%)	0 (0.0%)		2 (2.2%)
R0 resection, n (%)			0.782	
Yes	25 (69.4%)	36 (66.7%)		61 (67.8%)
No	11 (30.6%)	18 (33.3%)		29 (32.2%)
Curative resection, n (%)			0.259	
Yes	23 (63.9%)	28 (51.9%)		51 (56.7%)
No	13 (36.1%)	26 (48.1%)		39 (43.3%)
Specimen size, n (%)			0.004	
≤ 20 cm^2	23 (63.9%)	18 (33.3%)		41 (45.6%)
> 20 cm^2	13 (36.1%)	36 (66.7%)		49 (54.4%)
Max length, n (%)			0.03	
≤ 4 cm	6 (16.7%)	1 (1.9%)		7 (7.8%)
> 4 cm	30 (83.3%)	53 (98.1%)		83 (92.2%)
Dissection speed, median (IQR, cm^2/min)	0.19 (0.14)	0.25 (0.17)	0.012	0.23 (0.14)
Operative time, median (IQR, min)	99.50 (68.75)	103.00 (68)	0.422	100.50 (67)
Complications, n (%)				
Muscular damage	0 (0%)	0 (0%)	> 0.05	0 (0%)
Cardiac mucosal laceration	0 (0%)	0 (0%)	> 0.05	0 (0%)
Post-ESTD perforation	0 (0%)	0 (0%)	> 0.05	0 (0%)
Post-ESTD bleeding	4 (11.1%)	4 (7.4%)	0.821	8 (8.9%)
Post-ESTD fever	6 (16.7%)	10 (18.5%)	0.822	16 (17.8%)

IQR interquartile range

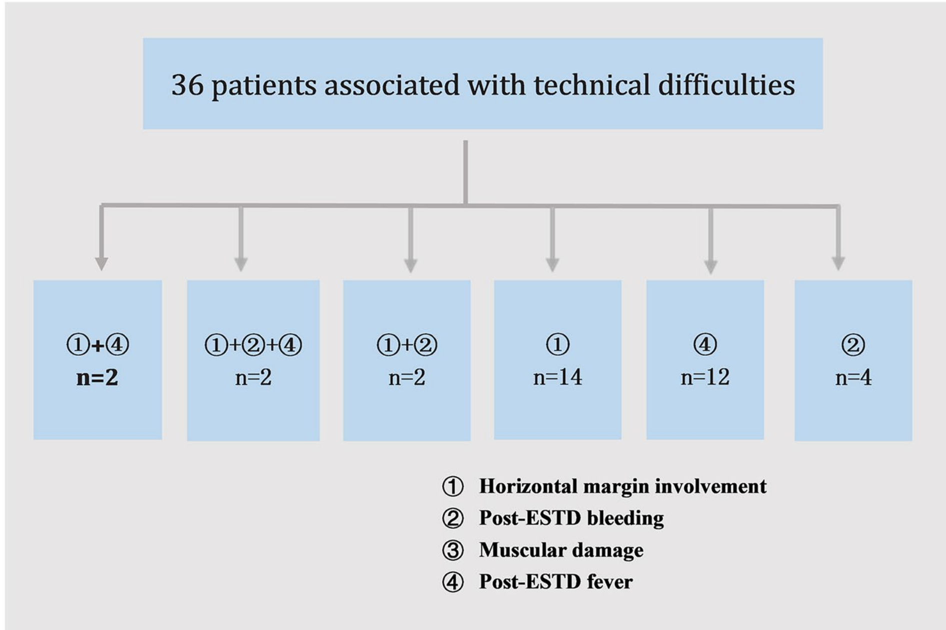

Fig. 2 Patients who experienced technical difficulties

stratify lesions that are more difficult and prone to failure of en bloc resection or adverse events. Univariate and multivariate logistic regression analyses were conducted for the risk factors that may lead to technical difficulties. As shown in Table 4, the univariate regression analysis indicated that among the T stage variables, compared with Tis stage, T1a stage (OR 0.247, 95% CI 0.075–0.811, P = 0.021) was negatively correlated with the occurrence of technical difficulties, whereas there was no significant difference for the T1b stage. The multivariate regression analysis demonstrated that among the circumferential extent variables, compared with lesions with circumferential extents ranging from 1/2 to 3/4, whole-circumferential lesions (OR 11.926, 95% CI 1.380–103.04, P = 0.024) were an independent risk factor for technical difficulties. Compared with T1a stage, T1a stage (OR 0.131, 95% CI 0.030–0.569, P = 0.007) was a protective factor against the occurrence of technical difficulties. No significant differences were observed for the other risk factors.

Long-term outcomes

Esophageal stenosis

After the resection of extensive esophageal lesions, the surgeons adopted different preventive measures for stenosis based on the postoperative wound conditions: 13 patients (14.4%) received no special treatment for the wound, 13 patients (14.4%) received hormone injection into the wound, 14 patients (15.6%) underwent endoscopic balloon dilation, 18 patients (20.0%) had esophageal stents placed, 26 patients (28.9%) underwent autologous skin grafting, and 6 patients (6.7%) received balloon dilation combined with hormone injection (Table 5). Close follow-up was conducted after the operation. By the end of the study period, a total of 54 patients had developed stenosis, with a stenosis rate of 60%. The median time to esophageal stenosis was 59.5 (39.75–100.25) days. In the single-tunnel group, the main preventive measures for esophageal stenosis were no treatment (30.6%) and implantation of esophageal stents (25%), whereas in the double-tunnel group, the main preventive measures were autologous skin grafting (44.4%), hormone injection (16.7%), and placement of esophageal stents (16.7%). There was a significant difference in the preventive measures adopted between the two groups (P < 0.001). However, in terms of the postoperative esophageal stenosis rate, although the double-tunnel group had a higher stenosis rate (64.8% vs. 52.8%), the difference between the two groups was not statistically significant (P = 0.253). Among the 54 patients who developed esophageal stenosis, the median time to esophageal stenosis was similar in both groups (64 days vs. 56 days), and there was no significant difference (P = 0.717, Table 5).

Owing to significant differences between the single-tube group and the double-tube group at the baseline level (the proportion of circumferential lesion extent and the measures for preventing stenosis), the conclusions obtained in the previous section may have been affected by selection bias. To further compare whether there were differences in the postoperative stenosis rate between the two groups, a subgroup analysis was conducted for the patients with whole-circumferential esophageal lesions (Fig. 3). As shown in Table 6, there were no significant differences between the two groups in terms of lesion area, maximum long diameter, or methods for preventing stenosis, indicating that the baseline values

Table 4 Univariate and multivariate analyses of risk factors for technical difficulties

Risk factor	No. of events	No. of patients	Univariate analysis			Multivariate analysis		
			Odds ratio	95% Confidence interval	P value	Odds ratio	95% Confidence interval	P value
Method, n								
Single-tunnel	14	36	Ref			Ref		
Double-tunnel	22	54	1.080	(0.456, 2.559)	0.861	0.482	(0.129, 1.802)	0.278
Specimen size, n								
≤ 20 cm^2	15	41	Ref			Ref		
> 20 cm^2	21	49	1.300	(0.555, 3.044)	0.546	0.998	(0.316, 3.155)	0.997
Max length, n								
≤ 4 cm	2	7	Ref			Ref		
> 4 cm	34	83	1.735	(0.318, 9.469)	0.525	1.813	(0.181, 18.161)	0.613
Circumferential-extent, n								
$\geq 1/2, < 3/4$	2	12	Ref			Ref		
$\geq 3/4, < 1$	11	25	3.929	(0.710, 21.749)	0.117	6.561	(0.865, 49.736)	0.069
$= 1$	23	53	3.833	(0.764, 19.224)	0.102	11.926	(1.380, 103.04)	0.024
Location, n								
Upper	2	9	Ref			Ref		
Middle	23	49	3.096	(0.584, 16.425)	0.184	5.039	(0.718, 35.357)	0.104
Lower	11	32	1.833	(0.324, 10.367)	0.493	2.334	(0.308, 17.659)	0.412
Macroscopic type, n								
IIa	11	27	Ref			Ref		
IIb	20	49	1.003	(0.386, 2.609)	0.995	0.581	(0.179, 1.884)	0.365
IIc	1	3	0.727	(0.059, 9.041)	0.804	0.850	(0.036, 19.859)	0.920
Mixed type	4	11	0.831	(0.195, 3.538)	0.802	0.312	(0.050, 1.947)	0.212
T stage, n								
Tis	10	16	Ref			Ref		
T1a	14	48	0.247	(0.075, 0.811)	0.021	0.131	(0.030, 0.569)	0.007
T1b	12	26	0.514	(0.144, 1.836)	0.306	0.237	(0.050, 1.125)	0.070
Operative time, n								
≤ 1 h	4	14	Ref			Ref		
> 1 h	32	76	1.818	(0.523, 6.319)	0.347	0.824	(0.159, 4.258)	0.817

Table 5 Comparison of postoperative management between 90 patients with single- and double-tunnel ESTD

Esophageal stenosis	Single-tunnel ESTD (n = 36)	Double-tunnel ESTD (n = 54)	P value	Total (n = 90)
Preventive measures for post-ESTD stenosis, n (%)			< 0.001	
Blank control	11 (30.6%)	2 (3.7%)		13 (14.4%)
Steroid injection	4 (11.1%)	9 (16.7%)		13 (14.4%)
Endoscopic balloon dilation	6 (16.7%)	8 (14.8%)		14 (15.6%)
Prophylactic stent placement	9 (25.0%)	9 (16.7%)		18 (20.0%)
Autologous skin-grafting surgery	2 (5.6%)	24 (44.4%)		26 (28.9%)
EBD combined with steroid	4 (11.1%)	2 (3.7%)		6 (6.7%)
Postoperative stenosis rate, n (%)			0.253	
Without stenosis	17 (47.2%)	19 (35.2%)		36 (40.0%)
With stenosis	19 (52.8%)	35 (64.8%)		54 (60.0%)
Time to stenosis, median (IQR, days)	64 (117)	56 (29)	0.717	59.5 (60.5)

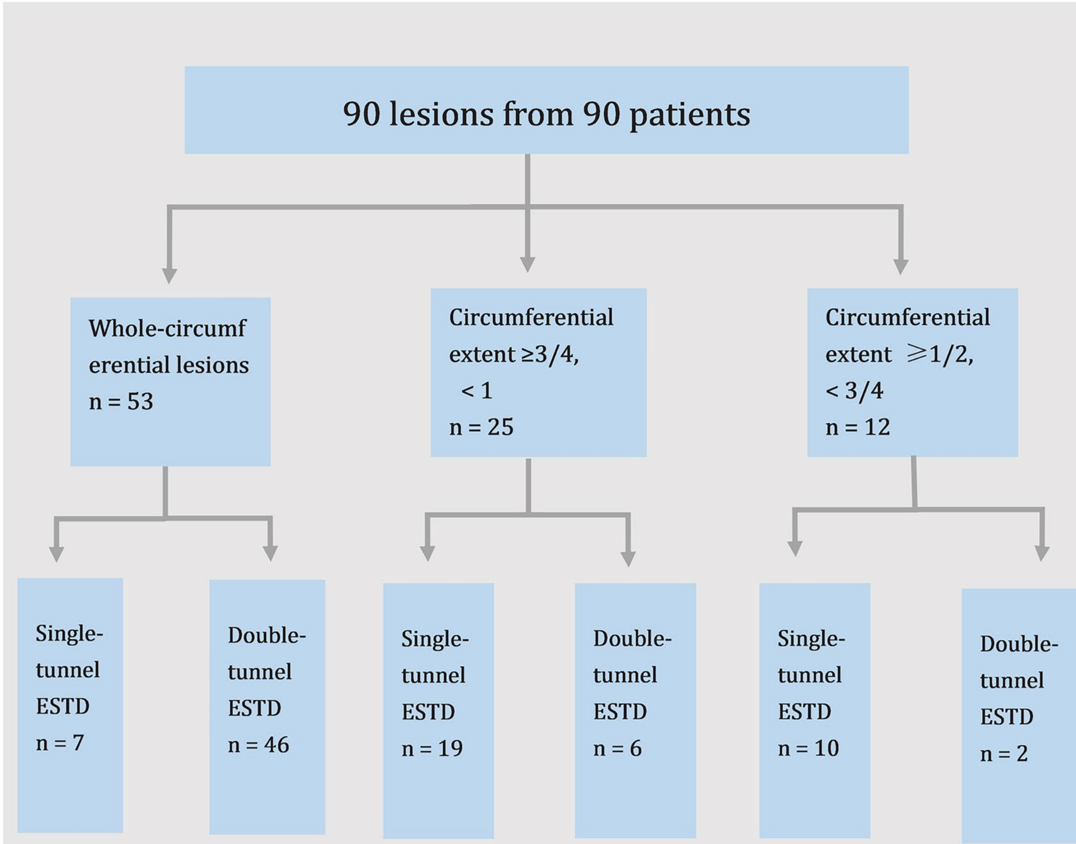

Fig. 3 Circumferential extent of the lesions and the treatment methods used in 90 patients

Table 6 Comparison of postoperative management between single- and double-tunnel ESTD for 53 patients with whole-circumferential lesions

Esophageal stenosis	Single-tunnel ESTD (n = 7)	Double-tunnel ESTD (n = 46)	P value	Total (n = 53)
Specimen size, n (%)			1.000	
≤ 20 cm^2	2 (28.6%)	15 (32.6%)		17 (32.1%)
> 20 cm^2	5 (71.4%)	31 (67.4%)		36 (67.9%)
Max length, n			0.249	
≤ 4 cm	1 (14.3%)	1 (2.2%)		2 (3.8%)
> 4 cm	6 (85.7%)	45 (97.8%)		51 (96.2%)
Preventive measures for post-ESTD stenosis, n (%)			0.058	
Blank control	1 (14.3%)	1 (2.2%)		2 (3.8%)
Steroid injection	0 (0.0%)	9 (19.6%)		9 (17.0%)
Endoscopic balloon dilation	2 (28.6%)	6 (13.0%)		8 (15.1%)
Prophylactic stent placement	3 (42.9%)	8 (17.4%)		11 (20.8%)
Autologous skin-grafting surgery	0 (0.0%)	20 (43.5%)		20 (37.7%)
EBD combined with steroid	1 (14.3%)	2 (4.3%)		3 (5.7%)
Postoperative stenosis rate, n (%)			1.000	
Without stenosis	3 (42.9%)	16 (34.8%)		19 (35.8%)
With stenosis	4 (57.1%)	30 (65.2%)		34 (64.2%)
Time to stenosis, median (IQR, days)	122 (202)	55.5 (34.5)	0.649	55.5 (52.5)

were comparable. The results revealed that there were no statistically significant differences between the two groups in terms of the postoperative stenosis rate or the median time of stenosis (P = 1.000, 0.649).

Survival

Overall survival (OS) was defined as the time from ESTD to death from any cause. Recurrence-free survival (RFS) was defined as the time from ESTD to the occurrence of distant or lymph node metastasis. Disease-specific survival (DSS) was defined as the time from ESTD to death from cancer recurrence. A total of 90 patients were included in this study, among whom 16 were lost to follow-up and 74 were successfully followed. There were 28 patients in the single-tunnel group and 46 in the double-tunnel group. Among the followed-up patients, 7 experienced successive recurrences. Five patients received corresponding treatments after recurrence (2 patients underwent ESD a second time, 2 patients underwent esophagectomy, and 1 patient received radiotherapy and chemotherapy) and are now in good condition. The other 2 patients who experienced esophageal cancer recurrence did not receive special treatment and later died with systemic metastasis. One patient died 6 months after single-tunnel ESTD, and the other died 36 months after double-tunnel ESTD. The remaining 67 patients had no recurrence (Fig. 4). As shown in Table 7, there were no statistically significant differences in the recurrence rate

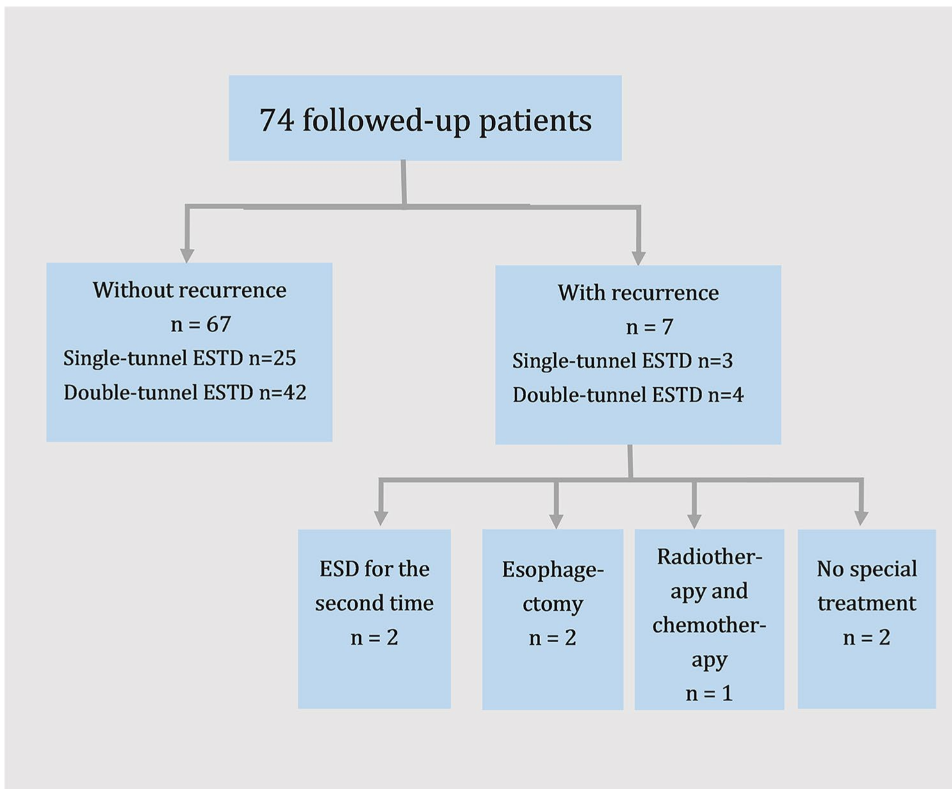

Fig. 4 Recurrence status and supplementary treatment modalities of 74 follow-up patients

Table 7 Comparison of long-term outcomes between single- and double-tunnel ESTD for 74 followed-up patients

Esophageal stenosis	Single-tunnel ESTD (n = 28)	Double-tunnel ESTD (n = 46)	P value	Total (n = 74)
Follow-up time, median (IQR, months)	33 (57.75)	63 (47.75)	0.229	60.5 (53.25)
Recurrence rate, n (%)			1.000	
Without recurrence	25 (89.3%)	42 (91.3%)		67 (90.5%)
With recurrence	3 (10.7%)	4 (8.7%)		7 (9.5%)
Time to recurrence, median (IQR, months)	15 (28)	26 (32.5)	0.649	15 (35)
Mortality rate, n (%)			1.000	
Death	1 (3.6%)	1 (2.2%)		2 (2.7%)
Survival	27 (96.4%)	45 (97.8%)		72 (97.3%)

(P = 1.000), recurrence time (P = 0.649) or mortality rate (P = 1.000) between the two groups. K−M survival analysis was conducted on the patients in both groups, and the results also revealed no significant differences in OS (P = 0.6242), DSS (P = 0.6242), or RFS (P = 0.6753) between the two groups (Fig. 5A–C).

Among the 74 patients who were followed up, 45 underwent curative resection, and 29 underwent noncurative resection. To eliminate the influence of noncurative resection on tumour recurrence, Kaplan−Meier survival analysis was further conducted on the RFS of patients who underwent curative resection. Among them, there were 20 patients in the single-tunnel group, with 2 cases of recurrence, and 25 patients in the double-tunnel group, with 2 cases of recurrence. The results revealed that there was still no statistically significant difference in RFS between the two groups (P = 0.7148, Fig. 5D).

Discussion

The results of this study indicate that ESTD is an effective treatment option for large early esophageal carcinoma, with an en bloc resection rate of 97.8%, an R0 resection rate of 67.8%, and a mean dissection speed of 0.23 cm^2/min, which is comparable to the results reported by Zhang et al. [6, 14]. For large early esophageal cancer, the main advantage of ESTD over ESD is that the submucosal injection fluid can remain in the submucosal layer for a longer time, reducing the injection volume and frequency and improving the efficiency and safety of dissection. Moreover, it can maintain a clear submucosal layer view, which helps to shorten the operative time and improve the resection efficiency [6]. In fact, several recent studies have reported that ESTD is faster than ESD in the treatment of superficial esophageal squamous cell carcinoma [4, 15–18].

This study compared the outcomes of single- and double-tunnel ESTD in the treatment of large esophageal lesions. The lesion area in the double-tunnel group was generally larger, making en bloc resection more challenging. However, the results revealed that the en bloc resection rate was greater in the double-tunnel group (100.0% vs. 94.4%, P = 0.307). Although the difference was not statistically significant, the double-tunnel technique demonstrated a more obvious advantage in treating large esophageal lesions, which are more challenging; the reason for this is that two narrow submucosal tunnels can support the endoscope tip, stabilizing the endoscope and facilitating parallel access to the muscular layer. The endoscope can push the lesion up from the submucosal tunnel, providing sufficient tension on the resection plane and enabling en bloc resection of large lesions in two steps. The lower R0 and curative resection rates in the double-tunnel group may be attributed to the larger lesion area, which increases the likelihood of horizontal and vertical cancer cell infiltration. It is difficult for surgeons to accurately determine the resection range based on endoscopic observation alone, leading to a greater risk of positive margins. Additionally, larger lesions have a greater chance of

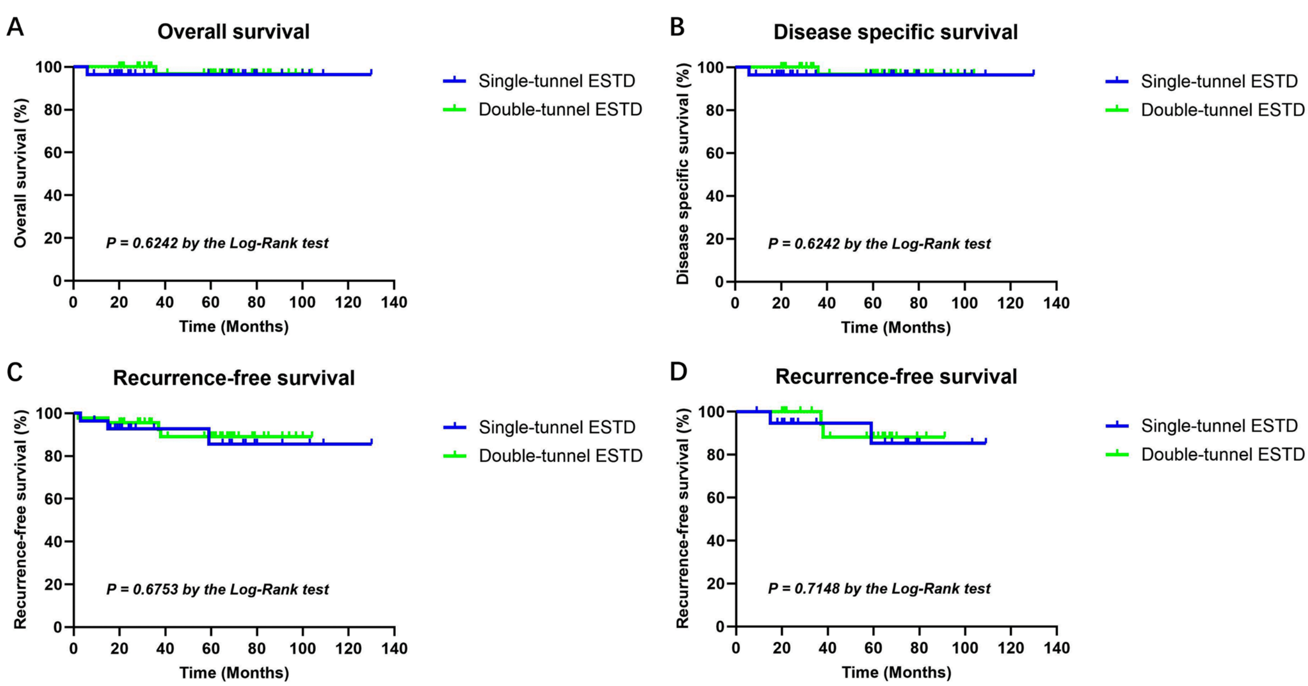

Fig. 5 **A−D** survival analysis of OS, DSS and RFS between the two groups

submucosal invasion exceeding 200 μm and a higher risk of lymph node metastasis [19, 20], which are also important reasons for considering noncurative resection. From a histological perspective, there were no significant differences in pathological results between the two groups, indicating the potential advantages of the double-tunnel technique in terms of resection quality and efficacy.

The results revealed that patients who underwent double-tunnel ESTD had a faster resection speed. According to the statistical results, the lesion area and maximum long diameter in the double-tunnel group were significantly larger than those in the single-tunnel group. This finding indicates that when dealing with larger lesions, surgeons tend to establish two submucosal tunnels, dividing a large lesion into two halves for submucosal dissection and achieving complete resection; this not only did not increase the operative time but also significantly improved the resection speed. As mentioned in previous studies, during single-tunnel ESTD treatment of whole-circumferential lesions, the mucosa begins to droop, the tunnel becomes loose, and as the surgeon starts to widen the tunnel, it becomes difficult to maintain sufficient traction during lateral submucosal dissection. Moreover, as the dissection proceeded laterally, this situation often became increasingly difficult. In contrast, in the double-tunnel ESTD procedure, owing to the narrower tunnels, tension and traction were maintained for a longer time [6]. In recent years, Zhu et al. [3, 14, 21] reported on endoscopic submucosal multitunnel dissection surgery, confirming the feasibility, effectiveness, and safety of this surgery for treating large superficial esophageal tumour lesions. The double-tunnel technique is more suitable for lesions with a high degree of circumferentiality, large area, and long diameter, ensuring more complete resection of the lesion and greater resection efficiency. For the same lesion, the double-tunnel technique can effectively shorten the operative time, thereby reducing the risk of potential surgical complications [22]. In this study, there was no significant difference in the incidence of short-term postoperative complications between the two techniques, indicating that double-tunnel ESTD is as safe and reliable as single-tunnel ESTD.

As shown in Table 1, for lesions with a circumferential extent of $\geq 1/2$ and $< 3/4$, single-tunnel ESTD resection was the main approach (10 vs. 2), and both surgical methods achieved a 100% en bloc resection rate. For lesions with a circumferential extent of $\geq 3/4$, double-tunnel ESTD treatment was the main approach (52 vs. 26). In the single-tunnel group, two patients failed to achieve en bloc resection, indicating that the en bloc resection rate of the double-tunnel group was superior to that of the single-tunnel group (100% vs. 92.3%). This finding seems to answer the question raised in previous studies; specifically, for lesions with a circumferential extent of $\geq 3/4$, it is recommended that patients undergo double-tunnel ESTD treatment. However, this conclusion still requires validation through studies with larger sample sizes.

Multivariate logistic regression analysis indicated that whole-circumferential lesions were an independent risk factor for technical difficulties, which was consistent with the results of Nagata's study [23], as the resection of whole-circumferential lesions requires greater operational skills and faces more complex and variable intraoperative situations. Interestingly, in the univariate analysis, T1a stage was negatively correlated with the incidence of technical difficulties, which contrasts with the findings of Nagata's study. However, when we included factors such as surgical methods in the multivariate analysis, T1a stage was still a protective factor against technical difficulties; we determined that this may be related to the small sample size of Tis and T1b stage patients, and no definite conclusions could be drawn. A larger sample size is needed to confirm this point.

After extensive esophageal lesion resection, the stenosis rate of wounds with a circumferential extent greater than 3/4 is 94% [24], and that of whole-circumferential wounds is nearly 100% [25]. According to the wound condition, preventive stenosis treatment is needed. In this study, the stenosis rate of wounds with a circumferential extent greater than 3/4 was 65.4%, which was lower than the results of previous studies, indicating that postoperative management is crucial for preventing stenosis. In addition, the patients in the double-tunnel group had mainly whole-circumferential lesions (85.2%), and the risk of postoperative stenosis was greater than that in the single-tunnel group. However, after preventive stenosis treatment, there was no significant difference in the incidence of stenosis or the median stenosis time between the two groups (Table 5), indicating that active postoperative management can effectively reduce the incidence of stenosis. To further eliminate the influence of baseline level differences on the results, a statistical analysis of whole-circumferential lesions was conducted (Table 6), and the results were consistent with the previous results. Therefore, it was concluded that there was no significant difference in the incidence of postoperative stenosis or the median stenosis time between the two groups. Given the advantages demonstrated by the double-tunnel ESTD as mentioned earlier, for early large esophageal carcinoma, especially those with a circumferential extent greater than 3/4 of the circumference, it is recommended to undergo double-tunnel ESTD treatment and take relevant measures to prevent esophageal stenosis. At the same time, more clinical studies are needed to verify this conclusion.

This is the largest multicentre evaluation to date examining both short- and long-term outcomes in this specific patient population treated with single- or double-tunnel super minimally invasive surgery. The study makes a valuable contribution to the understanding of optimal management strategies for large early esophageal carcinoma, particularly in the context of organ preservation. Furthermore, the SMIS through tunnel channel [26] is a highly reproducible and teachable treatment method. Up to now, this technique has been expanded to hundreds of hospitals across the whole country. However, this study also had certain limitations. First, this work adopted a retrospective design, which may lead to selection bias. Second, although the median follow-up time was 60.5 months, patients with very short follow-up times were also included. It is necessary to conduct longer follow-up studies and further prospective studies to confirm our results. Third, the proportion of Tis and T1b stage patients was lower than that of T1a stage patients, which may have affected the OR value and caused bias in the determination of risk factors. Finally, studies with larger sample sizes are still needed to clarify the specific application scope of the double-tunnel technique to provide a greater evidence-based medical basis for clinical workers.

In the future, we will conduct relevant randomized controlled trials, by including a larger sample size, to further verify our findings. We will also set up control groups such as the ESD group or the hybrid ESD group, to compare the differences between different groups and evaluate the efficacy of different surgical methods, providing data support and evidence-based medical basis for clinical workers to choose surgical methods.

Conclusion

ESTD is effective in treating large early esophageal carcinoma. Compared with the single-tunnel technique, the double-tunnel technique has a faster resection speed, and there is no significant difference in short-term postoperative complications or long-term follow-up results between the two groups. Therefore, double-tunnel ESTD is safe, reliable and more efficient in treating large EECs.

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Ethical approval This study was approved by the Medical Ethics Committee of Chinese PLA General Hospital (Ethics Approval No. S2023-188-01), and all methods were carried out in accordance with the Helsinki Declaration and its later amendments.

Informed consent All subjects gave written informed consent.

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