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Feasibility and strategy of common hepatic artery lymph node dissection in thoracolaparoscopic esophagectomy for thoracic esophageal squamous cell cancer

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Abstract

Controversy about the adequate extent of lymph node (LN) dissection persists in surgery for thoracic esophageal squamous cell carcinoma (ESCC). The present study estimates the feasibility and strategy of common hepatic artery LN dissection during ESCC surgery.

The clinical data of 482 patients with ESCC, who underwent thoracolaparoscopic esophagectomy at Fujian Medical University Union Hospital, were retrospectively selected. Among the 482 ESCC patients, 224 patients underwent thoracolaparoscopic esophagectomy with routine common hepatic artery LN dissection (cohort 1), while 258 patients underwent the same procedure without common hepatic artery LN dissection (cohort 2). The proposed operation method was introduced to safely dissect the common hepatic artery LN. Both univariate and multivariate analyses were performed to analyze the clinicopathological factors correlated to the common hepatic artery LN metastasis.

The main postoperative complications were pneumonia, anastomotic leakage, vocal cord palsy and cardiovascular disease. There was no significant difference in the incidence of major postoperative complications between the 2 cohorts ($P > .05$), and the incidence was similar in a number of reports. The metastatic rate of common hepatic artery LNs was 4.91%, which was relatively lower. Based on the logistic regression analysis of 5 factors, tumor location and T classification were risk factors for common hepatic artery LN metastasis ($P < .05$).

Routine common hepatic artery LN dissection is safe and feasible during a thoracolaparoscopic esophagectomy for ESCC. Although the metastatic rate is lower, common hepatic artery LN dissection should be performed for lower thoracic ESCCs, especially for tumors that invade the outer membrane.

Abbreviations: ESCC = esophageal squamous cell carcinoma, LN = lymph node, TNM = Tumor Node Metastasis, UICC = Union for International Cancer Control.

Keywords: common hepatic artery lymph node, esophagectomy, lymphadenectomy, thoracic esophageal cancer, thoracolaparoscopic

1. Introduction

Esophageal squamous cell carcinoma (ESCC) is a common malignant tumor worldwide.[1] At present, the outcome for patients with ESCC remains unsatisfactory. The high frequency and irregularity of lymph node (LN) metastasis is one of the primary reasons.[2] According to the 7th Tumor Node Metastasis (TNM) Classification and the Union for International Cancer Control (UICC) of Malignant Tumors, LN dissection is essential, and a 15-node dissection is required as a minimum.[3] In consideration of the frequency and risk of LN metastasis, an extended LN dissection may be strictly performed. However, a recent controversy has developed as to whether routine extended LN dissection should be performed for all stages of EC,[4] which may be associated with increased operative time, postoperative complication,[5] and damage to immune function.[6] In the present study, the feasibility and strategy of common hepatic artery LN dissection during thoracolaparoscopic esophagectomy were evaluated.

2. Patients and methods

2.1. Patients

The institutional review board of Fujian Medical University Union Hospital approved the present study. In the present study, 482 patients who underwent thoracolaparoscopic esophagectomy for thoracic ESCC at Fujian Medical University Union Hospital between January 2012 and July 2015 were selected. Among these patients, 224 patients underwent

esophagectomy with routine common hepatic artery LN dissection (cohort 1), while 258 patients underwent the same procedure without common hepatic artery LN dissection (cohort 2). The records of all cases were retrospectively reviewed. All cases underwent full preoperative disease staging. The staging was performed according to the 7th UICC TNM classification and was based on chest and abdomen enhanced computed tomography (CT), esophagoscopy, barium esophagography and neck color ultrasound. Positron emission tomography (PET) was also performed for the preoperative evaluation, when necessary. According to these examinations, patients with stage T1-T3 esophageal tumors, but had no distant metastases, were included in the present study. The exclusion criteria were as follows:

(I) patients with nonsquamous esophageal cancer;
(II) patients with cervical esophageal cancer or gastroesophageal junction cancer,
(III) patients receiving neoadjuvant chemotherapy and radiotherapy;
(IV) patients with distant metastasis;
(V) patients with double primary cancers.

2.2. Surgical technique

The surgery was performed in 3 stages. First, thoracoscopy was performed to mobilize the esophagus and dissect the mediastinal LNs.[7] Second, laparoscopy was performed to mobilize and create the gastric conduit. Lastly, a left cervical neck incision was performed to create a cervical esophagogastric anastomosis. The surgical procedures were similar in both groups.

In the second stage, the patient was placed in the supine position. Five ports were used: a 10-mm trocar below the umbilicus for the camera; a 12-mm trocar at the left subcostal for the ultrasonic scalpel and a 5-mm trocar on the right subcostal for the endo-forceps; two 5-mm trocars bilateral to the umbilicus for the endo-forceps. First, the gastrocolic omentum was divided with the ultrasonic scalpel, and the right gastroepiploic arcade was protected. The short gastric arteries were carefully divided to prevent accidental tearing of the spleen. The stomach was lifted to expose the nodes along with the celiac trunk. The left gastric artery was freed from the roots of the blood vessel, and the left gastric artery LNs were resected. Subsequently, the common hepatic artery LNs were thoroughly resected along the upper edge of pancreas and the surface of the common hepatic artery. During this procedure, attention was given to protect the hepatic artery, pancreas, and cisterna chyli from damage. Then, the left gastric vessels were divided using a haemo-lock clip.

2.3. Statistical analysis

Statistical analysis was performed to compare variables between the 2 groups. The X^2-test or Fisher exact test was used for discrete variables. Multiple logistic regression analysis was performed to evaluate the statistical significance of the differences in the effects of clinical factors in terms of tumor location, tumor length, pathological TNM stage, pathological T stage, and pathological N stage. All statistical analyses were performed using version 15.0 of the Statistical Package for Social Sciences (SPSS). A P value $<.05$ was considered statistically significant.

Table 1

Clinicopathologic characteristics of the patients.

Factor	Cohort 1 (224)	Cohort 2 (258)	*P* value
Gender			.593
Male	184	207	
Female	40	51	
Tumor location			.991
Upper	25	29	
Middle	154	176	
Lower	45	53	
P stage			.980
I	45	51	
II	76	86	
III	103	121	
Tumor invasion degree			.999
T1	60	69	
T2	73	84	
T3	89	103	
T4	2	2	
N classification			.998
N0	96	110	
N1	58	66	
N2	41	49	
N3	29	33	

Cohort 1, esophagectomy with common hepatic artery LN dissection; Cohort 2, esophagectomy without common hepatic artery LN dissection.

3. Results

3.1. Patient characteristics

A total of 482 patients, who underwent thoracolaparoscopic esophagectomy at Fujian Medical University Union Hospital, were included in the present study. The patients and the tumor characteristics are summarized in Table 1. These patients were divided into 2 cohorts. In cohort 1, patients ($n=224$) underwent thoracolaparoscopic esophagectomy with common hepatic artery LN dissection. Among these patients, 184 patients (82.15%) were male and 40 patients (17.85%) were female, and the average age of these patients was 59 years old. In cohort 2, patients ($n=258$) underwent thoracolaparoscopic esophagectomy without common hepatic artery LN dissection. Among these patients, 207 patients (80.23%) were male and 51 patients (19.77%) were female, and the average age of these patients was 58 years old. All patients were at stage I to III. There were no differences in clinical and pathological factors between these 2 groups.

3.2. LN metastasis

A total of 17,032 LNs were dissected (35 LNs per patient). In cohort 1, 588 common hepatic artery LNs were dissected (2 LNs per patient), only 11 patients had common hepatic artery LN metastasis, and the metastasis rate was 4.91%. Compared with other LNs, the metastatic rate of common hepatic artery LNs was lower (Table 2).

3.3. Risk factors for common artery LN

In the present study, the clinicopathological factors associated with the metastatic rate for common hepatic artery LNs were also analyzed (Table 3). Logistic regression analysis (Table 4) revealed that common hepatic artery LN metastasis was correlated to both the tumor location ($P<.0001$) and T classification ($P<.005$), but

Table 2

The regional lymph node metastatic rates in the 2 cohorts.

Locoregional lymph node	Cohort 1	Cohort 2	P value
Upper paraesophageal	12 (5.36%)	15 (5.81%)	.828
Left recurrent nerve	28 (12.50%)	30 (11.63%)	.769
Right recurrent nerve	35 (15.63%)	38 (14.73%)	.784
Subcarinal	20 (8.93%)	24 (9.30%)	.887
Middle paraesophageal	45 (20.09%)	56 (21.71%)	.664
Lower paraesophageal	30 (13.39%)	39 (15.12%)	.590
Left gastric artery	27 (12.05%)	36 (13.95%)	.537
Common hepatic artery	11 (4.91%)	/	.000

Cohort 1, esophagectomy with common hepatic artery LN dissection; Cohort 2, esophagectomy without common hepatic artery LN dissection.

Table 3

Risk factors for common hepatic artery LN metastasis.

Factor	common hepatic artery LN		
	metastasis	non-metastasis	P value
Tumor location			.000
Upper	0	25	
Middle	0	154	
Lower	11	34	
P stage			.118
I	0	45	
II	2	74	
III	9	94	
Tumor invasion degree			.002
T1	1	59	
T2	1	72	
T3	8	81	
T4	1	1	
N classification			.156
N1	3	55	
N2	3	38	
N3	5	24	
Tumor length (cm)			.458
$0 < L \leq 5$	8	174	
$L > 5$	3	39	

was not correlated to tumor size and N classification ($P > .05$). However, with the increase in N classification, the metastatic rate for common hepatic artery LNs exhibited a rising trend (N1: 5.17%; N2: 7.32%; N3: 17.24%).

3.4. Postoperative complications

There were no operative deaths in either of the 2 groups. Furthermore, the distribution of overall complications was 77 of 224 patients (34.37%) in cohort 1 and 84 of 258 patients (32.55%) in cohort 2 (Table 5). These complications included the following: pneumonia, anastomotic leakage, vocal cord palsy, gastrointestinal dysfunction, cardiovascular disease, and chylothorax.[8] There was no statistically significant difference in the incidence of major complications.

Table 5

Complications after thoracolaparoscopic esophagectomy in the 2 cohorts.

Complication	Cohort 1	Cohort 2	P value
Overall complication	77 (34.37%)	84 (32.55%)	.673
Pneumonia	24 (10.71%)	28 (10.85%)	.732
Anastomotic leakage	18 (8.04%)	25 (9.69%)	.525
Vocal cord palsy	20 (8.93%)	21 (8.13%)	.757
Gastrointestinal dysfunction	7 (3.13%)	6 (2.32%)	.589
Cardiovascular disease	21 (9.37%)	23 (8.91%)	.861
Chylothorax	4 (1.79%)	4 (1.55%)	.840
Urinary tract infection	3 (1.34%)	4 (1.55%)	.847

Cohort 1, esophagectomy with common hepatic artery LN dissection; Cohort 2, esophagectomy without common hepatic artery LN dissection.

4. Discussion

The overall 5-year survival rate after esophagectomy is only approximately 22% in ESCC.[9,10] In order to improve the outcomes, a multidisciplinary management approach was developed.[11] However, this remained unsatisfactory due to the high frequency and irregularity of LN metastasis. The 7th TNM classification emphasizes the importance of LN metastasis for prognosis.[3] However, the rate of metastasis to each LN station vastly differs, and the effectiveness of the dissection of different LN stations are not equally important.[12,13] Therefore, the extent of adequate LN dissection remains as a subject of debate.[14]

Abdominal LNs are still considered as regional LNs of esophageal cancer in the present staging system, and the metastatic rate is high. For example, in thoracic esophageal cancer, the metastatic rate of the celiac axis LN is 22.2% and the left gastric artery LN is 27.42%.[15] However, since the metastatic rate is low and the location is particular, only few studies on common hepatic artery LNs have been reported.

4.1. Feasibility

Open esophageal cancer resection is a complex surgical procedure associated with significant morbidity and mortality.[16] Thoracolaparoscopic esophagectomy has been more frequently applied to decrease the morbidity and mortality associated with esophageal cancer resection.[17,18] However, it is difficult to dissect common hepatic artery LNs during thoracolaparoscopic esophagectomy, particularly due to the location. In the experience of the investigators, the surgeon's operating station is located on the left side of the patient, while the assistant's station is located on the right. The assistant lifts the body of the stomach and squeezes the pancreas with 2 endo-forceps, in order to expose the nodes along with the celiac trunk. The surgeon frees the left gastric artery from the roots of the blood vessel and divides the left gastric artery LNs first. Then, the common hepatic artery LNs are dissected along the upper edge of the pancreas and the surface of common hepatic artery. In this

Table 4

Logistic regression analysis of factors correlated to common hepatic lymph node metastasis.

Factors	Regression coefficient	Standard error	Wald value	P value	OR	95% CI
Tumor location	3.477	1.098	10.031	.002	32.361	3.763–278.274
T	1.416	0.736	3.703	.032	4.120	1.274–17.431

process, it was noted that the endo-forceps cannot be used to directly squeeze the surface of the pancreas while preventing damage caused by the sharp surgical instrument. This can be avoided by holding the small gauze with the endo-forceps.

The main postoperative complications were pneumonia, anastomotic leakage, vocal cord palsy, gastrointestinal dysfunction, cardiovascular disease, and chylothorax. The percentage of overall complications was 34.37% in cohort 1 and 32.55% in cohort 2. No significant difference was found.

4.2. Strategy

Upper abdominal LN metastasis in patients with thoracic ESCC is a risk factor due to its high metastatic rate and its association with poor survival.[10,19] In the present study, the metastatic rate of the left gastric artery LN was 12.05% in cohort 1 and 13.95% in cohort two. The upper abdominal LNs should be reclassified as regional LNs. Hence, extensive LN dissection should be performed for accurate staging, and to reduce regional recurrence and increase long-term survival.[20]

Common hepatic artery LNs are located farther from the esophagus and near the cisterna chyli, which may result in chylous ascites.[21] The metastatic rate to common hepatic artery LNs is lower when compared with other LNs. Shim et al reported that the dissection of common hepatic artery LNs may be safely omitted for Stage T1 thoracic ESCC.[4] In the present study, the metastatic rate of common hepatic artery LNs was nearly as low as some studies, which was only 4.91%. In addition, there was a significant difference between tumor invasion and TNM staging (T1: 1.67%; T2: 1.37%; T3: 8.99%; T4: 50.00%). Furthermore, 1 of the 60 patients with common hepatic artery LN metastasis was at stage T1. During the process, the dissection of the common hepatic artery LN was safe, and no chylous ascites was experienced.

Among the 224 ESCC patients, 11 of 45 patients with lower ESCC had common hepatic artery LN metastasis, and none of the 179 patients with upper or middle ESCC had common hepatic artery LN metastasis. The reason may be that it is easier for metastasis to occur in the common hepatic artery LN due to its closer proximity to the tumor in lower ESCC. The logistic regression analysis revealed that the metastasis of the common hepatic artery LN was significantly correlated to tumor location ($P < .0001$) and T classification ($P < .005$), but was not correlated to tumor size and N classification ($P > .05$). However, with the increase in N classification, the metastatic rate to the common hepatic artery LN also increased (N1: 5.17%; N2: 7.32%; N3: 17.24%). Therefore, the dissection should be extended to the common hepatic artery LN during esophagectomy for lower thoracic ECC, especially for patients with stage T3-T4 tumors.

There were some limitations in this study, including the following:

(1) this was a retrospective study, and there was some bias although the 2 groups had a good comparability;
(2) the sample size of the groups was small, and a prospective randomized controlled study should be performed at a later stage.

5. Conclusion

In conclusion, routine thoracolaparoscopic esophagectomy with common hepatic artery LN dissection is technically feasible and safe. Tumor location and T classification were the independent predictors of common hepatic artery LN metastasis in the present study. Although the metastatic rate of the common hepatic artery LN is low, the common hepatic artery LN should be dissected during esophagectomy for lower thoracic ESCC, especially for patients with stage T3-T4 tumors.

Author contributions

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References

[1] Wani S, Sharma P. Challenges with endoscopic therapy for Barrett's esophagus. Gastroenterol Clin North Am 2015;44:355–72.
[2] Nishihira T, Sayama J, Ueda H, et al. Lymph flow and lymph node metastasis in esophageal cancer. Surg Today 1995;25:307–17.
[3] Ajani JA, D'Amico TA, Almhanna K, et al. National comprehensive cancer network. Esophageal and esophagogastric junction cancers, version 1. 2015. J Natl Compr Canc Netw 2015;13:194–227.
[4] Shim YM, Park JS, Lee M, et al. Can common hepatic artery lymph node dissection be safely omitted in surgery for clinical T1N0 thoracic esophageal squamous cell carcinoma? Dis Esophagus 2013;26:272–5.
[5] Zhai C, Liu Y, Li W, et al. A comparison of short-term outcomes between Ivor-Lewis and McKeown minimally invasive esophagectomy. J Thorac Dis 2015;7:2352–8.
[6] Keller SM, Adak S, Wagner H, et al. Mediastinal lymph node dissection improves survival in patients with stages II and IIIa non-small cell lung cancer. Eastern Cooperative Oncology Group. Ann Thorac Surg 2000;70:358–65.
[7] Lin J, Kang M, Chen C, et al. Thoracolaparoscopy oesophagectomy and extensive two-field lymphadenectomy for oesophageal cancer: introduction and teaching of a new technique in a high-volume centre. Eur J Cardiothorac Surg 2013;43:115–21.
[8] Lin J, Kang M, Chen S, et al. Feasibility and strategy for left tracheobronchial lymph node dissection in thoracolaparoscopic esophageal cancer surgery. Thorac Cancer 2016;7:202–3.
[9] Shimada H, Okazumi S, Matsubara H, et al. Surgical outcome after the clearance of abdominal metastatic lymph nodes in 138 patients with thoracic esophageal carcinoma. Am J Surg 2007;193:448–52.
[10] Chen G, Wang Z, Liu XY, et al. Abdominal lymph node metastasis in patients with mid thoracic esophageal squamous cell carcinoma. World J Surg 2009;33:278–83.
[11] Kayani B, Zacharakis E, Ahmed K, et al. Lymph node metastases and prognosis in oesophageal carcinoma—a systematic review. Eur J Surg Oncol 2011;37:747–53.
[12] Udagawa H, Ueno M, Shinohara H, et al. The importance of grouping of lymph node stations and rationale of three-field lymphoadenectomy for thoracic esophageal cancer. J Surg Oncol 2012;106:742–7.
[13] van der Schaaf M, Johar A, Wijnhoven B, et al. Extent of lymph node removal during esophageal cancer surgery and survival. J Natl Cancer Inst 2015;107:djv043.
[14] Zhang HL, Chen LQ, Liu RL, et al. The number of lymph node metastases influences survival and International Union Against Cancer tumor-node-metastasis classification for esophageal squamous cell carcinoma. Dis Esophagus 2010;23:53–8.
[15] Ma X, Li B, Yang S, et al. Extent of lymph node dissection: common hepatic artery lymph node dissection can be omitted for esophageal squamous cell carcinoma. J Thorac Dis 2014;6:S325–32.
[16] Birkmeyer JD, Siewers AE, Finlayson EV, et al. Hospital volume and surgical mortality in the United States. N Engl J Med 2002;346:1128–37.

[17] Guo W, Ma X, Yang S, et al. Combined thoracoscopic-laparoscopic esophagectomy versus open esophagectomy: a meta-analysis of oytcomes. Surg Endosc 2016;30:3873–81.

[18] Luketich JD, Pennathur A, Franchetti Y, et al. Minimally invasive esophagectomy: results of a prospective phase II multicenter trial the eastern cooperative oncology group (E2202) study. Ann Surg 2015;261: 702–7.

[19] Seto Y, Fukuda T, Yamada K, et al. Celiac lymph nodes: distant or regional for thoracic esophageal carcinoma? Dis Esophagus 2008;21:704–7.

[20] Kang CH, Kim YT, Jeon SH, et al. Lymphadenectomy extent is closely related to long-term survival in esophageal cancer. Eur J Cardiothorac Surg 2007;31:154–60.

[21] Yau KK, Siu WT, Li MK. Chylous ascites in a patient with esophageal carcinoma. Clin Gastroenterol Hepatol 2005;3:A33.