

CLINICAL STUDY ON THE PATTERN OF LYMPHNODE METASTASIS IN CARCINOMA OF ESOPHAGUS (AN ANALYSIS OF 200 CASES)

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Objective: To study the pattern of lymphnode metastasis in carcinoma of esophagus. **Methods:** 200 cases of resected esophageal cancer specimens were carefully examined pathologically. Lymphnode metastasis, its pathway and extent in relation to pathological changes were analyzed. **Results:** Lymphnode metastasis was mainly regional and extended vertically in both directions. Leaping-over metastasis was another feature. The deeper invasion by the tumor, the higher frequencies of metastasis development, and vice versa. However, leaping-over metastasis was more likely to occur where tumor invasion was less severe. **Conclusion:** Owing to the high frequency of lymphnode metastasis in the superior mediastinum and the widely spanned leaping-over metastasis, an operative approach by three incisions through right thoracotomy with excision of the whole segment of esophagus and anastomosis at cervical region was recommended, in order to dissect lymphnodes in the cervical, thoracic and abdominal regions and to leave less or no metastatic lymphnodes behind.

Key words: Esophageal neoplasms, Lymphatic metastasis, Lymphnode excision

Lymphnode metastasis is the most common metastatic way of esophageal cancer, and also is the most important recurrence and fatal factor. Investigating its regular pattern of metastasis, the findings may be taken as a practical significant guide in treating by operation or radiation. 200 cases of

resected esophageal cancer in our department from 1986 to 1994 were analyzed. The influences of different pathological changes to the pathway and extent of lymphnode metastasis were discussed, in order to find the pattern and feature of lymphnode metastasis, and analyze the clinical significance.

MATERIALS AND METHODS

The study on 200 patients had undergone esophageal cancer surgery. there were 148 males and 52 females. The age ranged from 30 to 76 years. According to the criteria of UICC(1987), 6, 47, 100 and 47 cases were located at cervical, upper, mid and lower thoracic esophagus respectively. 2, 45, 117, and 36 cases in T₁, T₂, T₃, T₄ period respectively. The operation for cervical esophagus was blunt esophageal dissection involved with stripping. The operation for upper and mid thoracic esophagus were resected through right thoracotomy and anastomosed at cervical region. The tumor at lower thoracic esophagus was resected through left thoracotomy and anatomized above or below aortic arch.

The lymphnode metastasis of esophageal cancer was very complicated, not only deeply seated, but also extended extensively, involving about 20 groups of cervical, thoracic and abdominal lymphnodes. Referring to the international rule of esophageal cancer, all lymphnodes were cleaned according to the lymphatic drainage region and registered as the usual 16 groups classification.

RESULTS

Among the 200 cases, there were lymphnode metastases in 109 cases, the metastasis rate was 54.5%. The total number of resected lymphnodes were 1660, and there were lymphnode metastases in 243 lymphnodes. The metastasis frequency was 14.6% and there were 8.3 resected lymphnodes per case.

Metastasis Frequency

The lymphatic metastasis frequency of the cervical lymphnode groups was more than 45%, being the highest in all groups. Those of the lateral parts of the thoracic esophagus, lateral part of cardia, left gastric artery and common hepatic artery were more than 10%. They were also the common metastatic lymphnode sites (Table 1).

Metastasis Rate

The lymphnode metastasis rates in the cases with cervical and upper thoracic segment esophageal cancer were more than 65%, and in the cases with mid and lower thoracic esophageal cancer were about 50%. There was a significant difference between them (Table 2).

The Segment of Lesion

The longer the segment of lesion, the higher frequency the lymphnode metastasis. In the group with the lesion length more than 5 cm, the metastasis rate was more than 60%, which was significantly higher than that in the group with the lesion length less than 5 cm ($\chi^2=15.9658, P<0.005$).

Table 1. The location of esophageal cancer and the metastasis frequencies of each group of lymphnodes

Lymphnodes		Tumor location				Total
		Cervical 6 cases	Upper thoracic 47 cases	Mid thoracic 100 cases	Lower thoracic 47 cases	
No.	Group					200 cases
101	cervical paraesophageal	4/6(66.7) 4	2/9 (22.2) 2	4/7 (57) 3		10/22 (45.5) 9
102	deep cervical		3/11 (27.3) 2	6/7 (85.7) 3	1/1(100) 1	10/19 (52.6) 6
104	supraclavicular	1/1 (100) 1	1/4 (25) 1	2/2 (100) 2		4/7 (57.1) 4
105	upper thoracic paraesophageal		21/106 (19.8) 18	14/52 (26.9) 7	5/5 (100) 2	40/163 (24.5) 27
106	thoracic paratracheal		10/66 (15.2) 9	3/59 (5) 3	2/13 (15.4) 2	15/138 (10.9) 14
107	bifurcation		5/49 (10.2) 5	16/129 (8.3) 11	3/9 (33.3) 3	24/250 (9.6) 19
108	middle thoracic paraesophageal		0/3	51/303 (16.8) 29	1/25 (4) 1	52/331 (15.7) 30
109	pulmonal hilar		0/2	5/59 (8.5) 4	4/31 (12.9) 4	9/92 (9.8) 8
110	lower thoracic paraesophageal		0/4	1/31(3.2) 1	24/136 (17.6) 18	25/171 (14.6) 19
1, 2	right and left cardiac		0/13	10/77 (13) 7	11/68 (16.2) 6	21/158 (13.3) 13
3	lesser curvature		0/24	7/75 (9.3) 5	2/19 (10.9) 2	9/118 (7.6) 7
4	greater curvature		0/1	0/31	0/8	0/40
7	left gastric artery		0/9	9/10 (10) 7	13/38 (34.2) 6	22/137 (16.1) 13
8	common hepatic artery			2/7 (28.6) 2		2/7 (28.6) 2
9	celiac artery			0/3		0/3
10	plenic hilar			0/4		0/4
Total		5/7(71.4)4	42/301(14) 32	130/999(13) 49	66/353(18.7) 24	243/1660(14.6)109

The number of each group in the Table is: number of metastasis lymphnodes/number of resected lymphnodes (metastasis frequency %) number of cases with metastasis

The Relation Between Pathological Pattern And Metastasis Rate

Among the 200 cases, 192 cases belonged to the squamous epithelial carcinoma. The lower the grade of

differentiation, the higher the metastasis rate (Table 3). There were leaping-over metastases occurred in the 2

cases of lower thoracic esophageal non-differentiated small cell neoplasms.

Table 2. The relation between the tumor size (length) and lymphnodes metastasis rate

Tumor length	Lymphnodes metastasis rate				
	Cervical	Upper thoracic	Mid thoracic	Lower thoracic	Total
L < 3 cm		100% (2/2)	20% (1/5)	(0/3)	30% (3/10)
3 ≤ L < 5 cm	75% (3/4)	42.9% (6/14)	33.3% (12/36)	37.5% (6/16)	38.6% (27/70)
5 ≤ L < 7 cm	50% (1/2)	73.9% (17/23)	55.6% (15/27)	66.6% (10/15)	64.2% (43/67)
L ≥ 7 cm		87.5% (7/8)	65.6% (21/32)	61.5% (8/13)	67.9% (36/53)
Total	66.7% (4/6)	68.1% (32/47)	49% (49/100)	51.1% (24/47)	54.5% (109/200)

Metastasis Direction

In spite of easy metastasizing to the lateral esophageal lymphnodes, the upper thoracic esophageal cancers usually metastasized upwards, the mid and lower thoracic esophageal cancers metastasize vertically, but the former was usually upwards and the

latter was usually downwards (Table 4). Statistical treatment showed that the difference was significant ($\chi^2=0.9469$, $0.01 < P < 0.05$). The higher the position of lesion, the more frequency metastasized to cervical and thoracic lymphnodes. The lower the position of lesion, the more frequency metastasized to abdominal lymphnodes.

Table 3. The relation between the grade of differentiation of squamous epithelial carcinoma and the lymphnodes metastasis

Grade of differentiation	Lymphnodes metastasis rate				
	Cervical	Upper thoracic	Mid thoracic	Lower thoracic	Total
Well		42.9% (3/7)	(0/1)	37.5% (3/8)	
Moderate	80% (4/5)	69.7% (32/46)	49.4% (43/87)	50% (20/40)	55.6% (99/178)
Poor	(0/1)	100% (1/1)	100% (4/4)	83.3% (5/6)	

Metastasis Pattern

The lymphnode metastasis pattern could be divided into: (1) no metastasis; (2) regional metastasis: only occurred in the first lymphnode station; (3) leaping-over metastasis: there was no metastasis occurred in the first lymphnode station, but it occurred in the second or distant lymphnode stations; (4) consecutive metastasis; metastases occurred in the first, second and distant lymphnode stations. It was shown from the Table 5, there was a positive correlation between the depth of invasion and metastasis pattern ($\chi^2=52.6586$, $P < 0.005$). The 2 cases with tumor cell embolus in lymphatic vessel and blood vessel at

esophageal wall appeared leaping-over metastasis.

The Relation between the Position of Lesion and the Metastasis Pattern

Refers to Table 4.

The Depth of Tumor Invasion

There was no significant relation between the direction of lymphnode metastasis and the depth of tumor invasion, difference was not insignificant according to the statistical treatment ($\chi^2=3.2900$, $P > 0.05$).

Table 4. The relation between the tumor location and the patterns of lymphnode metastasis

Tumor location	Cases	Patterns of lymphnode metastasis								Directions of lymphnode metastasis						
		No		Regional		Leaping-over		Consecutive		Upwards		Both		Downwards Non-regional metastasis		
		Cases	%	Cases	%	Cases	%	Cases	%	Cases	%	Cases	%	Cases	Num.	
Cervical	6	2	33.3	4	66.7	0	0	0	0	0	0	0	0	0		
Upper	47	15	31.9	27	57.4	4	8.5	1	2.1	5	100.0	0	0	5		
middle	100	51	51.0	23	23.0	14	14.0	12	12.0	13	50.0	3	11.5	10	38.5	26
lower	47	23	48.9	11	23.4	7	14.9	6	12.8	1	7.7	6	46.2	6	46.2	13
Total	200	91		65		25		19		19	43.2	9	20.5	16	36.4	44

Table 5. The relation between the depth of tumor invasion and the patterns, directions of lymphnode metastasis

Depth of tumor invasion	Cases	Pattern of lymphnode metastasis								Direction of lymphnode metastasis						
		No		Regional		Leaping-over		Consecutive		Upwards		Both		Downwards Non-regional metastasis		
		Cases	%	Cases	%	Cases	%	Cases	%	Cases	%	Cases	%	Cases	%	cases Num.
T1	2	1	50.0	0		1	50.0	0		1	100.0					1
T2	45	30	66.7	7	15.6	6	13.3	2	4.4	3	37.5	1	12.5	4	50.0	6
T3	117	59	50.4	34	29.1	16	13.7	8	6.8	10	41.7	4	16.7	10	41.7	24
T4	36	1	2.8	24	66.7	2	5.6	9	25.0	5	45.5	4	36.4	2	18.2	11
Total	200	91	45.5	65	32.5	25	12.5	19	9.5	19	43.2	9	20.5	16	36.4	44

DISCUSSION

The Effect of Lymphnode Excision

The degree of lymphnode metastasis is an important factor, which effects the result of the surgical treatment of esophageal cancer. A large amount of data demonstrated that the lymphnode metastasis exerted a tremendous influence on the prognosis and lymphnode excision was important in operation.

The Pathway of Lymphnode Metastasis

The pathway of lymphnode metastasis in esophageal cancer is nearly the same as the pathway of normal lymphatic drainage. Because the esophageal lymphatic drainage is mainly in the vertical direction, the number of vertical lymphatic vessels is 6 times more than the horizontal lymphatic vessels, lymphnode metastasis is mainly regional and extends vertically in both directions. First, the metastasis extends to the paraesophageal lymphnodes nearby the tumor, and then to the deep cervical lymphnodes and

supraclavicular lymphnodes of the cervical segment. The upper thoracic esophageal cancer mainly extends up to the cervical lymphnodes along the esophagus. The mid thoracic esophageal cancer extends upwards not only to the upper thoracic paraesophageal lymphnodes, paratracheal lymphnodes, even the cervical lymphnode groups, but also downwards to the lateral part of cardiac and left gastric arteric lymphnodes, mainly in upward direction. The lower thoracic esophageal cancer mainly extends in downward direction, though may also extend in upward direction. Generally, the lymphatic drainage, is vertically flowed in both directions in the esophageal lymphatic vessels. The parts flowing down finally drain to the thoracic duct by way of abdominal lymphnodes, and then to the supraclavicular lymphnodes. It is not directly drained to the thoracic duct from the tumor region.

The Pathological Factors of Metastasis

The pathological factors influencing the lymphnode metastasis: It is usually that the bigger (longer) the tumor body, the deeper the tumor invasion,

and the lower the degree of differentiation, the easier the lymphnode metastasis.

In view of the relation between the depth of tumor invasion and lymphnode metastasis, we found that in the cases with distant metastasis (no regional metastasis), the ratio of occurring leaping-over metastasis and consecutive metastasis was 1:0 in T₁, 3:1 in T₂, 2:1 in T₃ and 2:9 in T₄. These meant that the deeper the tumor invasion, the higher the frequency of the consecutive metastasis and vice versa. However, leaping-over metastasis was more likely to occur where tumor invasion was less severe. There are abundant lymphatic vessels along the esophageal vertical axis in the deep esophageal mucosa and submucosa, and the lymphatic vessels connect each other. The lateral vessels of lymphatic vessel net in submucosa can pass through the esophageal muscular layer to the adventitious layer and connect with the lateral lymphatic vessels, which connect with each lateral esophageal lymphnodes. In the early phase, when the tumor cell invades to the lymphatic vessels in the deep esophageal mucosa and sub-mucosa, the tumor cells can flow vertically in both directions and metastasize to the distant lymphnodes. That is the leaping-over lymphnode metastasis. When tumor invades the esophageal adventitious layer the tumor not only extends to the lymphatic vessels in deep mucosa and submucosa, but also invades the deep lymphatic vessels in the adventitious layer of muscular layer. For this reason, the frequency of consecutive metastasis increases with the leaping-over metastasis. If tumor cell or tumor cell embolus gets away from the main nidus by way of lymphatic stream and stops in another lymphatic vessels, the new tumor occurs, i.e., the leaping-over metastasis happened in the esophageal wall. In this group there were 3 cases with new niduses away from the original tumor, the longest distance of new tumor from the original one was 14cm.

The feature of wide spanned leaping-over metastasis reminded us that the cases with long distance lymphnode metastasis cannot be considered as contraindication to operation, and the lymphnodes

cleaning should be massive. The idea is unsuitable that if the tumor is small and with less severe invasion, the lymphnode should be cleaned regionally or not.

The Operative Approach and Lymphnode Excision

Wherever the tumor is in the upper, mid or lower thoracic segment, the frequency of lymphnode metastasis in the superior mediastinum is very high. If operation is done through left thoracotomy approach, because of the block of aortic arch and descending left subclavicular artery, it is very difficult to excise the lymphnodes sharply in the superior mediastinum.

An operative approach by three incisions through right thoracotomy with excision of the whole segment of esophagus and anastomosis at cervical region is recommended, in order to dissect lymphnodes in the cervical, thoracic and abdominal regions and to leave less or no metastatic lymphnodes behind.

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