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表浅型食管鳞癌发生淋巴结转移的危险因素

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[摘　要] **目的：**分析表浅型食管鳞癌(superficial esophageal squamous cell carcinoma，SESCC)发生淋巴结转移(lymph node metastasis，LNM)与临床病理特征的关系，探讨SESCC发生LNM的相关危险因素。**方法：**回顾性分析2013年1月至2017年6月于南京军区总医院行手术治疗的215例SESCC患者，分析患者的性别、年龄、肿瘤部位、肿瘤大小、大体分型、分化程度、浸润深度、脉管癌栓浸润等临床病理特征。采用单因素分析SESCC LNM与其临床病理特征间的关系，采用logistic回归模型分析SESCC发生LNM的独立危险因素。**结果：**215例SESCC患者中有21例有LNM，淋巴结转移率为9.8%。单因素分析显示肿瘤最大直径、肿瘤浸润深度、组织学分化程度、脉管癌栓浸润与SESCC LNM具有相关性(均P<0.05)。采用logistic回归模型进行多因素分析结果显示，肿瘤最大直径、分化程度、浸润深度、脉管癌栓浸润均是SESCC发生LNM的独立危险因素(OR分别为5.632，5.570，5.401，4.316，均P<0.05)。**结论：**肿瘤最大直径、分化程度、浸润深度、脉管癌栓浸润均与SESCC LNM密切相关，术前需充分评估LNM的风险，选择最佳的治疗方法。

[关键词] 表浅型食管癌；淋巴结转移；临床病理特征；危险因素

Risk factors of lymph node metastasis in superficial esophageal squamous cell carcinoma

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Abstract **Objective:** To investigate the relationship between lymph node metastasis (LNM) and clinicopathological features in superficial esophageal squamous cell carcinoma (SESCC), and to explore the risk factors of LNM in SESCC. **Methods:** A total of 215 SESCC patients who underwent curative esophagectomy and lymphadenectomy in Nanjing General Hospital of Nanjing Military Command from January 2013 to June 2017, were retrospectively reviewed. Clinicopathological features of patients' gender, age, tumor location, tumor size, macroscopic type, differentiation degree, depth of tumor invasion and lymphovascular invasion were analyzed retrospectively. Univariate analysis was used to analyze the relationship between LNM and the clinicopathological features in

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SESCC. Logistic regression analysis was taken to analyze the independent risk factors of LNM in SESCC. **Results:** Among 215 patients with SESCC, 21 patients had LNM, the metastasis rate was 9.8%. Univariate analysis showed that the tumor size, depth of invasion, differentiation degree, and lymphovascular invasion were correlated with LNM in SESCC (all $P<0.05$). Logistic regression analysis showed that the tumor size, tumor differentiation, depth of invasion, lymphovascular invasion were all independent risk factors for LNM in SESCC (OR were 5.632, 5.570, 5.401, 4.316 respectively, all $P<0.05$). **Conclusion:** The tumor size, tumor differentiation, depth of invasion and lymphovascular invasion are closely correlated with LNM in SESCC. The risk of LNM in SESCC must be fully assessed to choose the optimal treatment.

Keywords superficial esophageal; lymph node metastasis; clinicopathological features; risk factors

表浅型食管鳞癌(superficial esophageal squamous cell carcinoma，SESCC)是指浸润局限于黏膜层或者黏膜下层的鳞癌，无论是否有淋巴结转移(lymph node metastasis，LNM)。其中无LNM者称为早期食管癌(early esophageal cancer，EEC)。EEC的治疗方法包括内镜下切除和外科手术治疗，内镜下切除方法主要包括内镜黏膜切除术(endoscopic mucosal resection，EMR)和内镜黏膜下剥离术(endoscopic submucosal dissection，ESD)。研究[1-2]发现：与传统外科手术相比，对无LNM的SESCC，内镜下切除具有创伤小、并发症少、恢复快、费用低等优点，且二者疗效相当，5年生存率可达85%~95%。但对于有LNM的SESCC病例，内镜下切除则无法达到根治效果，需按进展期癌进行手术治疗。因此术前对LNM风险的评估对SESCC治疗方法选择至关重要。本研究通过回顾性分析南京总医院外科手术治疗的SESCC患者的临床及病理资料，旨在探讨SESCC发生LNM的相关危险因素，为SESCC治疗方法的选择提供临床实践指导。

1 对象与方法

1.1 对象

回顾性分析2013年1月至2017年6月于南京总医院行手术治疗的215例SESCC患者的临床及病理资料。其中男137例，女78例，年龄44~91(63.94±7.88)岁。根据有无发生LNM情况，将SESCC患者分为有LNM组和无LNM组，分析比较两组患者的临床及病理特征。

1.2 主要观察指标

观察指标包括患者性别、年龄、肿瘤部位、肿瘤最大直径、大体类型、分化程度、浸润深度、脉管有无癌栓浸润等临床病理特征。相关定义和分类标准参照日本食道学会(Japan Esophageal Society，JES)指南[3]及我国食管癌规范化诊治指南[4]。根据病灶在食管的位置将其分为胸上段、中段、下段。大体分型将浅表型食管癌(type 0)分为：0~I型(隆起型)指肿瘤明显高出周围正常黏膜或呈息肉状外观；0~II型(平坦型)指癌组织无明显隆起或凹陷；0~III型(凹陷型)指癌组织较周围黏膜明显凹陷但不超过黏膜下层。按肿瘤浸润深度分为：M1期癌指病变仅局限于上皮内，未突破基底膜者，即原位癌/重度异型增生；M2期癌指病变突破基底膜，浸润黏膜固有层；M3期癌指病变浸润黏膜肌层但未突破黏膜肌层；SM期癌指病变浸润至黏膜下层，未达固有肌层。依据癌组织学分化程度，分为高分化、中分化、低分化。

1.3 统计学处理

运用SPSS 20.0统计软件进行数据分析，临床病理特征与LNM的关系的单因素分析采用χ^2检验或Fisher确切概率检验，采用logistic回归模型进行表浅食管鳞癌LNM独立危险因素分析。$P<0.05$为差异有统计学意义。

2 结果

2.1 临床病理特征

215例SESCC患者中，发生LNM者21例，淋巴结转移率为9.8%。其中年龄≤60岁者148例(68.8%)，>60岁者67例(31.2%)。215例SESCC患者中，胸上段14例(6.5%)、胸中段106例(49.3%)、胸下段95例(44.2%)；肿瘤最大直径<21 mm 104例(48.4%)、21~30 mm 64例(29.8%)、>30 mm 47例

(21.8%)；0~I型63例(29.3%)、0~II型118例(54.9%)、0~III型34例(15.8%)；高分化型88例(40.9%)、中分化型72例(33.5%)、低分化型55例(25.6%)；M1型58例(27.0%)、M2型13例(6.0%)、M3型74例(34.4%)、SM型70例(32.6%)；脉管查见有癌栓者13例(6.0%，表1)。

表1 215例SESCC的临床病理特征

Table 1 Clinicopathological features of 215 cases of SESCC

病理因素	*n*	LNM个数	淋巴结转移率/%	χ^2	*P*
性别				1.565	0.211
男	137	16	11.7		
女	78	5	6.4		
年龄/岁				0.051	0.281
≤60	148	14	9.5		
>60	67	7	10.4		
肿瘤位置				—	0.390
胸上段	14	0	0.0		
胸中段	106	10	9.4		
胸下段	95	11	11.6		
最大直径/mm				—	<0.001*
<21	104	2	1.9		
21~30	64	8	12.5		
>30	47	11	23.4		
大体分型				—	0.970
0~I	63	6	9.5		
0~II	118	12	10.2		
0~III	34	3	8.8		
分化程度				—	<0.001*
高	88	1	1.1		
中	72	7	9.7		
低	55	13	23.6		
浸润深度				—	0.036*
M1	58	0	0		
M2	13	1	7.7		
M3	74	9	12.2		
SM	70	11	15.7		
脉管有无癌栓				30.503	<0.001
无	202	14	6.9		
有	13	7	53.8		

* 采用 Fisher 确切概率法。

*Fisher exact probability method.

2.2 SESCC 发生 LNM 的单因素分析

单因素分析结果显示：肿瘤最大直径、分化程度、浸润深度、脉管有无癌栓浸润与SESCC LNM有关(均P<0.05)，而性别、年龄、肿瘤部位、大体分型与表浅型食管癌发生LNM无关(均P>0.05，表1)。

2.3 SESCC 发生 LNM 的多因素分析

Logistic回归分析结果显示：肿瘤最大直径、分化程度、浸润深度、脉管癌栓浸润均是SESCC LNM的独立危险因素(表2)。

2.4 肿瘤分化程度、直径大小与浸润深度的关系

多因素分析显示：肿瘤浸润深度是LNM的独立危险因素，通过判断浸润深度可有效预测LNM的风险。χ^2检验结果显示：肿瘤浸润深度与肿瘤大小、分化程度、脉管癌栓浸润密切相关(表3)。

表2 215例SESCC淋巴结转移的多因素分析

Table 2 Multivariate analysis of lymph node metastasis in 215 cases of SESCC

项目	B	SE	Wald	OR	95% CI	*P*
肿瘤最大直径	1.792	0.553	8.904	5.632	1.481~16.441	0.002
分化程度	1.703	0.761	8.361	5.570	1.527~17.022	0.001
浸润深度	1.686	0.509	8.737	5.401	1.137~16.083	0.010
脉管癌栓	1.545	0.647	5.630	4.316	1.459~12.240	0.004

表3 肿瘤分化程度、直径大小与浸润深度的关系

Table 3 Relationship between tumor differentiation, diameter size and depth of invasion

病理特征	*n*	M	SM	χ^2	*P*
肿瘤直径/mm				16.295	<0.001
<21	104	84	20		
≥21	111	61	50		
分化程度				33.917	<0.001
高	88	76	12		
中	72	31	41		
低	55	38	17		
脉管癌栓				5.292	0.021
无	202	140	62		
有	13	5	8		

3 讨论

食管鳞癌因黏膜下脉管组织丰富，容易出现LNM，既往文献[5-9]关于淋巴结转移率报道不一，表浅型食管癌的淋巴结转移率大致为5.0%~38.2%，其中食管M1期癌基本无转移，M2期癌中淋巴结转移率在0%~5%，M3期癌淋巴转移率约10%，SM期癌为10%~50%。在本研究中，215例SESCC患者有LNM者21例，淋巴结转移率为9.8%，其中M1期癌淋巴结转移率为0，M2期癌淋巴结转移率为7.7%，M3期癌淋巴结转移率为12.2%，SM期癌淋巴结转移率为15.7%，与国内外文献[6,10-12]报道基本相符。在本研究中，M2期淋巴结转移率为7.7%(1/13)，高于既往研究[13]，

此例患者为低分化鳞癌，脉管发现有癌栓浸润，考虑可能与此高危因素有关。近年来随着内镜技术的发展，EEC的检出率明显提高，EMR，ESD等内镜切除方法已成为EEC治疗的新选择，而有无LNM则是表浅型食管癌患者选择治疗方法的关键因素，然而术前尚无十分确切的对LNM评估的检查方法。因此，对SESCC患者临床病理特征进行分析显得十分必要。

本研究单因素分析结果显示：肿瘤最大直径、分化程度、浸润深度、脉管有无癌栓浸润均与SESCC LNM有关，而患者性别、年龄、肿瘤位置、大体分型等与LNM无关，这与国内外相关文献[14-16]的结论基本一致。本研究多因素分析显示：肿瘤最大直径、分化程度、浸润深度、脉管癌栓浸润均是SESCC LNM的独立危险因素，而肿瘤浸润深度又与肿瘤大小、分化程度、脉管癌栓浸润情况密切相关，且肿瘤直径越大、分化程度越低、脉管发生癌栓浸润者，肿瘤浸润深度越深，越容易发生LNM。在本研究中，M1期食管癌均无LNM，M2期仅有1例发生LNM，提示对于浸润至M1~M2的EEC，因其发生淋巴结转移率低，可以首选采取内镜下ESD治疗，可减少外科手术的相关风险和并发症，提高患者生存质量。对于肿瘤浸润至M3~SM期者，淋巴结转移率明显高于M1，M2，采取内镜下治疗前需要充分评估LNM风险。这与我国中国EEC筛查及内镜诊治专家共识[11,17]意见基本相符。有学者[7]将SM细分为SM1，SM2，SM3，并报道了淋巴结转移率会随浸润深度的增加而不断升高，SM2及SM3期癌的淋巴结转移率明显高于SM1。由于EEC的检出率不断提高，内镜下切除与外科食管癌根治术相比，并发症少、患者术后的生活质量高，且疗效相当，有学者[18-20]主张：对于术前评估没有明显LNM的M3~SM1期癌患者可行诊断性ESD治疗，术后应对切除标本仔细评估，必要时再追加食管癌根治术及放化疗。Wang等[21]研究发现：对于T1期食管癌(即M~SM期癌)患者，采取内镜下治疗并不会增加随后的食管癌根治术的手术难度、并发症的发生率，同时也不会影响食管根治术后的存活率，建议对表浅型食管癌患者可先采取内镜下治疗，根据术后标本情况再决定是否追加手术治疗。

对于食管SM2，SM3期癌，因其发生LNM的概率较高，可达30%~56%以上，故不推荐行内镜下治疗[11,22]。但由于本研究局限于对外科手术病理的回顾性分析，未能够按癌组织浸润深度将SM癌细分为SM1，SM2，SM3，进而逐一评估其发生LNM的风险，且本研究为小样本量研究，未来仍需大样本病例进一步研究分析。

综上所述，表浅型食管癌治疗方法的选择主要取决于肿瘤浸润深度，对于M1，M2期SESCC，因淋巴结转移率低，可采取内镜下治疗。对于M3~SM期SESCC，术前需充分评估其LNM风险，如脉管无癌栓浸润、分化程度高、肿瘤最大直径小于20 mm，则可考虑先采取诊断性内镜下ESD治疗，术后需充分评估标本情况，必要时追加外科手术或放射、化学治疗。

参考文献

1. Joo DC, Kim GH, Park DY, et al. Long-term outcome after endoscopic submucosal dissection in patients with superficial esophageal squamous cell carcinoma: a single-center study[J]. Gut Liver, 2014, 8(6): 612-618.
2. Yamashina T, Ishihara R, Nagai K, et al. Long-term outcome and metastatic risk after endoscopic resection of superficial esophageal squamous cell carcinoma[J]. Am J Gastroenterol, 2013, 108(4): 544-551.
3. Japan Esophageal Society. Japanese Classification of Esophageal Cancer, 11th edition: part I[J]. Esophagus, 2017, 14(1): 1-36.
4. 中国抗癌协会食管癌专业委员会. 食管癌规范化诊治指南[M]. 北京: 中国协和医科大学出版社, 2013: 1-171.
   China Anticancer Association Committee for Esophageal Cancer. Standardized guideline for the diagnosis and treatment of esophageal cancer[M]. Beijing: China Union Medical University Press, 2013: 1-171.
5. Barret M, Prat F. Diagnosis and treatment of superficial esophageal cancer[J]. Ann Gastroenterol, 2018, 31(3): 256-265.
6. Duan XF, Tang P, Shang XB, et al. The prevalence of lymph node metastasis for pathological T1 esophageal cancer: a retrospective study of 143 cases[J]. Surg Oncol, 2018, 27(1): 1-6.
7. Sgourakis G, Gockel I, Lang H. Endoscopic and surgical resection of T1a/T1b esophageal neoplasms: a systematic review[J]. World J Gastroenterol, 2013, 19(9): 1424-1437.
8. Pennathur A, Farkas A, Krasinskas AM, et al. Esophagectomy for T1 esophageal cancer: outcomes in 100 patients and implications for endoscopic therapy[J]. Ann Thorac Surg, 2009, 87(4): 1048-1054; discussion 1054-1055.
9. Kuwano H, Nishimura Y, Oyama T, et al. Guidelines for diagnosis and treatment of carcinoma of the esophagus April 2012 edited by the Japan Esophageal Society[J]. Esophagus, 2015, 12: 1-30.
10. 段晓峰, 尚晓滨, 唐鹏, 等. T1期食管癌淋巴结转移的预后因素

分析[J]. 中华外科杂志, 2017, 55(9): 690-695.
DUAN Xiaofeng, SHANG Xiaobin, TANG Peng, et al. Lymph node metastasis and prognostic factors for T1 esophageal cancer[J]. Chinese Journal of Surgery, 2017, 55(9): 690-695.

11. 中华医学会消化内镜学分会消化系早癌内镜诊断与治疗协作组, 中华医学会消化病学分会消化道肿瘤协作组, 中华医学会消化病学分会消化病理学组. 中国早期食管鳞状细胞癌及癌前病变筛查与诊治共识(2015年, 北京)[J]. 中华消化内镜杂志, 2016, 33(1): 3-18.
Chinese Medical Association Digestive Endoscopy Branch, Digestive System Early Diagnosis and Treatment of Early Cancer, Collaborative Team, Chinese Medicine Association of Digestive Diseases, Digestive Tract Oncology Group, Chinese Medical Association Digestive Disease Branch Digestive Pathology Group. The consensus of screening, diagnosis and treatment of early esophageal squamous cell carcinoma and precancerous lesions in China (2015, Beijing)[J]. Chinese Journal of Digestive Endoscopy, 2016, 33(1): 3-18.
12. 杨海军, 雷瑞雪, 段国婕. 表浅食管癌淋巴结内转移相关病理因素探讨[J]. 中国实用医药, 2014, 9(9): 62-64.
YANG Haijun, LEI Ruixue, DUAN Guojie. The pathological factors of lymph node metastasis in superficial esophageal carcinoma[J]. China Practical Medicine, 2014, 9(9): 62-64.
13. Sepesi B, Watson TJ, Zhou D, et al. Are endoscopic therapies appropriate for superficial submucosal esophageal adenocarcinoma? An analysis of esophagectomy specimens[J]. J Am Coll Surg, 2010, 210(4): 418-427.
14. 李苗, 曾晓清, 谭黎杰, 等. 浅表食管癌术后患者的生存及预后分析[J]. 中华医学杂志, 2016, 96(6): 460-463.
LI Miao, ZENG Xiaoqing, TAN Lijie, et al. Survival and prognostic evaluation of superficial esophageal cancer after surgery[J]. National Medical Journal of China, 2016, 96(6): 460-463.
15. Moon JY, Kim GH, Kim JH, et al. Clinicopathologic factors predicting lymph node metastasis in superficial esophageal squamous cell carcinoma[J]. Scand J Gastroenterol, 2014, 49(5): 589-594.
16. Mitobe J, Ikegami M, Urashima M, et al. Clinicopathological investigation of lymph node metastasis predictors in superficial esophageal squamous cell carcinoma with a focus on evaluation of lympho-vascular invasion[J]. Scand J Gastroenterol, 2013, 48(10): 1173-1182.
17. 中国抗癌协会肿瘤内镜专业委员会中华医学会消化内镜学分会. 中国早期食管癌筛查及内镜诊治专家共识意见(2014年, 北京)[J]. 中华消化内镜杂志, 2015, 32(4): 205-224.
China Anticancer Association Cancer Endoscopy Professional Committee Chinese Medical Association Digestive Endoscopy Branch. Expert consensus opinion on early esophageal cancer screening and endoscopic diagnosis and treatment in China (2014, Beijing)[J]. Chinese Journal of Digestive Endoscopy, 2015, 32(4): 205-224.
18. 刘敏, 黄蕊, 刘志国. 术前考虑为M3~SM1层的食管表浅鳞癌是否适于内镜下治疗[J]. 中华消化内镜杂志,2017, 34(6): 381-384.
LIU Min, HUANG Rui, LIU Zhiguo. Whether the esophageal superficial squamous cell carcinoma considered as M3~SM1 layer before surgery is suitable for endoscopic treatment[J]. Chinese Journal of Digestive Endoscopy, 2017, 34(6): 381-384.
19. Min YW, Lee H, Song BG, et al. Comparison of endoscopic submucosal dissection and surgery for superficial esophageal squamous cell carcinoma: a propensity score-matched analysis[J]. Gastrointest Endosc, 2018, Epub ahead of print.
20. Huang R, Cai H, Zhao X, et al. Efficacy and safety of endoscopic submucosal tunnel dissection for superficial esophageal squamous cell carcinoma: a propensity score matching analysis[J]. Gastrointest Endosc, 2017, 86(5): 831-838.
21. Wang S, Huang Y, Xie J, et al. Does delayed esophagectomy after endoscopic resection affect outcomes in patients with stage T1 esophageal cancer? A propensity score-based analysis[J]. Surg Endosc, 2018, 32(3): 1441-1448.
22. Japan Esophageal Society. Japanese classification of esophageal cancer, 11th edition: part II and III[J]. Esophagus, 2017, 14(1): 37-65.

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