

胸段食管鳞癌颈部淋巴结转移特点及其 临床意义

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[摘要] 背景与目的: 食管癌颈部淋巴结转移率较高, 但少有专门报道。本研究分析胸段食管鳞癌颈部淋巴结转移特点, 探讨其临床意义。方法: 选择1993年1月—2003年12月在福建省肿瘤医院行胸段食管鳞癌三野淋巴结清扫根治术患者1 131例, 对术后病理证实颈部淋巴结转移患者376例的具体情况进行分析。结果: 全组颈部淋巴结转移率为33.2%, 其中胸上、中及下段的颈部淋巴结转移率分别为43.7%、33.0%和16.0%。单因素分析显示, 颈部淋巴结转移率与肿瘤部位、病理分化程度、病变X线长度、pT分期以及淋巴结转移个数有关($P<0.05$), 但多因素回归分析显示, 颈部淋巴结转移率只与肿瘤部位、pT分期及淋巴结转移个数有关($P<0.05$)。颈段食管旁淋巴结转移最多见, 其次是锁骨上淋巴结转移, 颈深淋巴结及咽后淋巴结转移少见; 胸上、中及下段的颈部淋巴结转移数占该段淋巴结总转移数的比率分别为57.7%、32.0%和10.0%, 差异有统计学意义($P<0.05$); 各段食管癌右颈部淋巴结转移多于左颈部。结论: 影响胸段食管鳞癌颈部淋巴结转移独立因素是肿瘤部位、pT分期及淋巴结转移数; 颈段食管旁淋巴结转移最多见, 其次是锁骨上淋巴结转移, 颈深淋巴结及咽后淋巴结转移少见。

[关键词] 食管肿瘤; 颈部淋巴结转移; 淋巴结转移数; 淋巴结转移率

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Clinical analysis of the characteristics of cervical lymph node metastasis in thoracic esophageal squamous cell carcinoma CHEN Jun-qiang¹, ZHENG Xiong-wei², ZHU Kun-shou³, LI Jian-cheng¹, LIN Yu¹, PAN Cai-zhu¹, PAN Jian-ji¹ (1. Department of Radiation Oncology, Fujian Provincial Tumor Hospital, Teaching Hospital of Fujian Medical University, Fuzhou Fujian 350014, China; 2. Department of Pathology, Fujian Provincial Tumor Hospital, Teaching Hospital of Fujian Medical University, Fuzhou Fujian 350014, China; 3. Department of Thoracic Surgery, Fujian Provincial Tumor Hospital, Teaching Hospital of Fujian Medical University, Fuzhou Fujian 350014, China)

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[Abstract] **Background and purpose:** Lymph node (LN) metastasis of esophageal cancer of neck rate higher, but there is little bulk reports. This article aimed to analyze the characteristics of cervical lymph node metastasis (CLN) in thoracic esophageal squamous cell carcinoma (TE-SCC) and the clinical role. **Methods:** A total number of 1 131 TE-SCC patients underwent radical esophagectomy plus three-field lymph node dissection at Fujian Provincial Tumor Hospital between Jan. 1993 to Dec. 2003, during which, 367 patients had pathological metastasis of CLN. **Results:** The metastatic rate of CLN was 33.2% for the entire group, 43.7%, 33.0% and 16.0% for the upper, middle and lower TE-SCC respectively. Single factor analysis showed that the metastatic rate of CLN was relevant with the tumor site, pathological differentiated degree, lesion length showed in X-ray, pT stage and the number of CLN ($P<0.05$). But multivariate regression analysis showed that the metastatic rate of CLN was just relevant with the tumor site, pT stage and the number of CLN ($P<0.05$). Metastasis of cervical paraesophageal lymph nodes was the most common, and

supraclavicular lymph node metastasis was next, and metastasis of cervical profound lymph nodes and retropharyngeal lymph nodes were rare. The ratio of the number of CLN occupied the sum of the segmental CLN were 57.7%, 32.0% and 10.0% for the upper, middle and lower TE-SCC respectively ($P<0.05$). Right CLN of each segmental TE-SCC was more than left CLN. **Conclusion:** Independent factors on CLN in TE-SCC are the tumor site, pT stage and the number of CLN. Metastasis of cervical paraesophageal lymph nodes is the most common, and supraclavicular lymph node metastasis is next, and metastasis of cervical profound lymph nodes and retropharyngeal lymph nodes are rare.

[Key words] Esophageal neoplasm; Cervical lymph node metastasis; Number of lymph node metastasis; Rate of lymph node metastasis

淋巴结转移是食管癌最常见的转移途径,特别是颈部具有较高的转移率(23.4%~49.5%)^[1-4]。近20年来随着外科进展,下颈、右胸、上腹三野淋巴结清扫的食管癌根治术成为胸段食管癌的主要治疗手段,该术式手术暴露好,淋巴结清扫彻底,能够较为真实体现淋巴结转移情况^[1,5]。目前有关胸段食管鳞癌颈部淋巴结转移特点少有专门报道,本研究对1 131例胸段食管鳞癌三野淋巴结清扫根治术中有颈部淋巴结转移的376例进行回顾性分析,结果报道如下。

1 资料和方法

1.1 病例选择

入组条件:①须福建省肿瘤医院收治的首程治疗行颈部、右胸部、上腹部三野淋巴结清扫的胸段食管癌根治术,且清除淋巴结总数 ≥ 15 个;②术前体检双颈及锁骨上区未扪及肿大淋巴结;③未行术前放疗或化疗;④术后病理诊断为鳞癌,无远处脏器转移。

1.2 手术方法

经右胸后外侧切口、上腹正中切口、下颈部U字形切口行全胸段食管合并贲门及部分小弯切除,大弯侧胃管经食管床于颈部与食管行吻合术,清除双下颈锁骨上、

纵隔、上腹部引流区淋巴结,以右喉返神经起始部为界划分颈部淋巴结和纵隔淋巴结^[1]。根据日本食管疾病淋巴结分组标准^[6],颈部淋巴结包括101(颈段食管旁淋巴结)、102(下颈深淋巴结)、103(咽后淋巴结)、104(锁骨上淋巴结),左、右侧分别用R、L表示。

1.3 统计学处理

应用SPSS 15.0统计软件分析资料,定量资料组间比较采用方差检验,定性资料组间比较采用 χ^2 检验,多因素采用Logistic回归分析。 $P<0.05$ 为差异有统计学意义。

2 结 果

2.1 各段食管癌锁骨上区域淋巴结转移特点

1993年1月—2003年12月符合入组条件患者共1 131例,术后病理证实有颈部淋巴结转移376例。全组共清除淋巴结28 227枚,平均每例清除淋巴结25.0枚(15~73枚),淋巴结阳性总数2 418枚,总转移度为8.6,其中胸上段、胸中段及胸下段的淋巴结转移度分别为6.9、8.9和8.9;各段淋巴结总清除数及淋巴结转移总数差异无统计学意义($P>0.05$),但各段在颈部、纵隔及腹部淋巴结转移数差异有统计学意义($P<0.05$),其中胸上段、胸中段及胸下段的颈部淋巴结转

表 1 1 131例胸段食管癌各段淋巴结转移特点比较

Tab. 1 Characteristics of 1 131 patients with TE-SCC

Variables	Total	Upper	Middle	Lower	F	P
n(%)	1131(100.0)	183(16.2)	848(75.0)	100(8.8)		
Total dissected LN	28227	4714	21046	2467	0.997	0.369
Average dissected LN (range)	25.0(15-73)	25.8(15-68)	24.8(15-71)	24.7(15-73)		
Positive LN [n(%)]	2418	324(13.4)	1874(77.5)	220(9.1)	1.069	0.344
Supraclavicular positive LN [n(%)]	808(33.4)	187(57.7)	599(32.0)	22(10.0)	6.065	0.002
Mediastinal positive LN [n(%)]	1038(42.9)	120(37.0)	845(45.1)	73(33.2)	3.465	0.032
Abdominal positive LN [n(%)]	572(23.7)	17(5.2)	430(22.9)	125(56.8)	26.800	<0.000 1
Metastatic ratio/%	8.6	6.9	8.9	8.9		

移数在该段所占比率分别为57.7%、32.0%和10.0%，差异有统计学意义($P < 0.05$ ，表1)。

全组颈部淋巴结转移率为33.2%，其中胸上段、胸中段及胸下段的颈部淋巴结转移率分别为43.7%、33.0%和16.0%($P < 0.0001$)，术后(pT)分期的T₁、T₂、T₃及T₄颈部淋巴结转移率分别为18.6%、29.1%、34.5%和42.2%。各段在101L组、101R组和104R淋巴结转移率差异有统计学意义($P < 0.05$ ，表2)。

2.2 颈部淋巴结转移率与临床因素关系

单因素分析显示，颈部淋巴结转移率与肿瘤部位、病理分化程度、病变X线长度、pT分期以及淋巴结转移数差异有统计学意义($P < 0.05$)，与性别及年龄差异无统计学意义($P > 0.05$ ，表3)。但多变量Logistic回归分析显示，颈部淋巴结转移率只与肿瘤部位、pT分期及淋巴结转移数有关($P < 0.0001$ ，表4)。

表2 367例颈部淋巴结阳性具体部位转移率[例(%)]

Tab. 2 Number of cervical lymph node metastasis in 367 patients

Variables	Total	Upper	Middle	Lower	χ^2	[n(%)]
						P
Total	376(100.0)	80(43.7)	280(33.0)	16(16.0)	22.461	< 0.0001
101L	120(10.6)	33(18.0)	82(9.7)	5(5.0)	14.740	0.001
101R	262(23.2)	54(29.5)	198(23.3)	10(10.0)	13.890	0.001
102L	10(0.9)	2(1.1)	8(0.9)	0(0.0)	1.017	0.601
102R	7(0.6)	3(1.6)	4(0.5)	0(0.0)	4.020	0.134
103	3(0.3)	2(1.1)	1(0.1)	0(0.0)	5.700	0.058
104L	44(3.9)	8(4.4)	35(4.1)	1(1.0)	2.475	0.290
104R	63(5.6)	15(8.2)	47(5.5)	1(1.0)	6.372	0.041

表3 颈部淋巴结转移率与临床因素关系单因素分析

Tab. 3 Univariate analysis of prognostic factors of cervical LNM

Variable	Case	No. with LNM	No. without LNM	χ^2	[n(%)]
					P
Total patients	1131	376(33.2)	755(66.8)		
Gender				2.806	0.094
Male	803	279 (34.7)	524(65.3)		
Female	328	97(29.6)	231(70.4)		
Age/year				0.496	0.481
< 60	723	235(32.5)	488(67.5)		
≥ 60	408	141(34.6)	267(65.4)		
Tumor location				22.461	< 0.0001
Upper TE	183	80(43.7)	103(56.3)		
Middle TE	848	280(33.0)	568(67.0)		
Lower TE	100	16(16.0)	84(84.0)		
Differentiation status				16.071	< 0.0001
Low	207	82(39.6)	125(60.4)		
Intermediate	657	231(35.2)	426(64.8)		
High	267	63(23.6)	204(76.4)		
lesion length by X-ray/cm				4.721	0.030
≤ 5	626	191(30.5)	435(69.5)		
> 5	505	185(36.6)	320(63.4)		
pT stage				11.090	0.011
T ₁	59	11(18.6)	48(81.4)		
T ₂	213	62(29.1)	151(70.9)		
T ₃	769	265(34.5)	504(65.5)		
T ₄	90	38(42.2)	52(57.8)		
No of LNM				454.977	< 0.0001
0	478	0(0.0)	478(100.0)		
1-2	342	160(46.8)	182(53.2)		
3-6	225	148(65.8)	77(34.2)		
≥ 7	86	68(79.1)	18(20.9)		

LNM: Lymph node metastasis.

表 4 颈部淋巴结转移与临床因素关系多因素Logistic回归分析

Tab. 4 Multiple logistic regression analysis of prognostic factors of cervical LNM

Variable	Regression coefficient <i>B</i>	<i>S.E</i>	<i>Wald</i>	<i>HR(95%CI)</i>	<i>P</i>
Tumor location (upper, middle and lower TE)	-1.139	0.179	40.484	0.320(0.226-0.455)	< 0.000 1
Differentiation status(low, intermediate, high)	-0.010	0.131	0.006	0.990(0.765-1.281)	0.939
Lesion length by X-ray (≤ 5 cm, > 5 cm)	-0.028	0.165	0.029	0.972(0.703-1.345)	0.865
pT stage (T_{1-4})	-1.892	0.208	82.522	0.151(0.100-0.227)	< 0.000 1
No of LNM (0, 1-2, 3-6, ≥ 7)	0.444	0.030	223.680	1.560(1.471-1.653)	< 0.000 1

3 讨 论

食管癌是我国最常见的恶性肿瘤之一, 死亡率位居第4位, 食管鳞癌是主要的病理类型, 占95%以上, 且绝大多数发生于胸段食管^[7]。由于胸段食管癌淋巴结转移具有明显的上下双向转移和跳跃性转移特点, 特别是颈部具有较高的淋巴结转移率^[1]。目前对于手术是否要进行颈部淋巴结清扫, 放疗是否要包括颈部淋巴结引流区预防照射, 国内外学者仍存在争议, 尚无共识。2009年公布的第7版AJCC食管癌分期中将淋巴结转移个数作为N分期的标准^[8], 了解胸段食管鳞癌颈部淋巴结转移特点, 对指导食管癌分期、放疗靶区的设计以及手术方式有非常重要的临床意义。

颈部是早、晚期食管癌常见的淋巴结转移部位, Igaki等^[9]报道黏膜下浸润的胸段食管癌颈部淋巴结转移率高达17%; Koide等^[10]报道 T_2 或 T_3 的胸中段食管癌颈部淋巴结转移率为27.4%; 本研究 T_1 、 T_2 、 T_3 及 T_4 的胸段食管癌颈部淋巴结转移率分别为18.6%、29.1%、34.5%和42.2%。肿瘤部位是食管癌颈部淋巴结转移最主要因素, Akiyama等^[2]报道290例食管癌三野淋巴结清扫根治术, 总颈部淋巴结转移率为31.0%, 其中胸上段、中段及下段分别为46.3%、29.2%和27.2%; Ando等^[3]报道116例食管癌三野淋巴结清扫根治术, 总颈部淋巴结转移率为28.0%, 胸上段、中段及下段分别为39.0%、26.0%和24.0%。本研究总颈部淋巴结转移率为33.2%, 胸上段、中段及下段的颈部淋巴结转移率分别为43.7%、33.0%和16.0% ($P < 0.000 1$), 与文献报道的数据大致相同^[2-3]。

纵隔喉返神经旁淋巴结转移与颈部淋巴结转移有明显相关性, Shimada等^[11]报道喉返神经旁淋巴结转移是颈淋巴结转移与否的独立预测因子。Tabira等^[12]报道喉返神经旁淋巴结有无转移其颈部淋巴结转移率分别为43.5%和11.1%; Yoshioka等^[13]也报道有无喉返神经旁淋巴结转移者的颈部淋巴结转移率分别为51.6%和11.6%。本研究单因素分析显示, 颈部淋巴结转移率与肿瘤部位、病理分化程度、病变X线长度、pT分期以及淋巴结转移数有关 ($P < 0.05$), 但多因素Logistic回归分析显示, 颈部淋巴结转移率只与肿瘤部位、pT分期及淋巴结转移数有关 ($P < 0.05$)。本研究结果表明, 颈部淋巴结转移率随肿瘤位置升高和总体淋巴结转移数的增加而增高, 建议对于胸上段食管癌和淋巴结转移数较多者, 应常规给予颈部淋巴结转移部位的治疗。

近年来开展的食管癌调强适形放疗, 可以提高生存率并减少放疗并发症^[14], 但如何确定颈部淋巴结引流区亚临床病灶是放疗难点。本研究发现颈部淋巴结转移有2个特点: ①颈段食管旁淋巴结是最常见的转移部位, 其次是锁骨上淋巴结, 颈深淋巴结及咽后淋巴结少见, 转移与病变部位有关, 部位越下转移率越低; ②各段食管癌右颈部淋巴结转移明显多于左颈部, 与Akiyama等^[2]报道相似。建议对胸上段食管癌在勾画放疗靶区时应包括左右颈段食管旁及锁骨上淋巴结引流区, 对胸中段及下段食管癌应酌情处理。

与传统胸腹两野清扫术相比, 胸段食管癌颈胸腹三野淋巴结清扫术能提高生存率和降低术后局部复发率, 但常规三野淋巴结清扫因有较高的手术并发症而限制其广泛应用^[2-3]。根

据本研究结果和文献报道建议对以下患者常规行颈部淋巴结清扫术：①胸上段食管癌^[15]；②颈部彩超显示颈部淋巴结短径 ≥ 0.5 cm^[16]；③喉返神经旁淋巴结转移者^[11-13]。

综上所述，胸段食管鳞癌颈部淋巴结转移率较高，肿瘤部位、pT分期及淋巴结转移数是影响颈部淋巴结转移独立因素；颈段食管旁淋巴结转移最多见，其次是锁骨上淋巴结转移，颈深淋巴结及咽后淋巴结转移少见；各段食管癌右颈淋巴结转移明显多于左颈转移。

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