



· 论 著 ·

709例鼻咽癌颈部各区淋巴结转移的相关性分析

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[摘要] **背景与目的:** 基于鼻咽癌颈部各区淋巴结转移相关性的放疗临床靶区 (clinical target volume, CTV) 勾画研究尚未见报道。回顾性分析709例鼻咽癌患者颈部各区淋巴结转移间的相关性, 为鼻咽癌基于颈部各区淋巴结转移相关性的放疗靶区勾画提出初步意见。**方法:** 纳入2011年12月—2018年6月在西部战区总医院经病理学检查确诊并伴有颈部淋巴结转移的鼻咽癌患者709例, 基于2013年新版《头颈部肿瘤颈部淋巴结分区指南》分析颈部各区淋巴结转移与其余各淋巴结区之间的相关性, 采用 χ^2 检验和logistic回归模型进行分析。**结果:** 淋巴结转移概率最高的前4位依次是: II b (82.79%)、VII a (82.65%)、II a (60.50%)、III区 (43.86%), 相关性分析显示, I b区淋巴结转移与II a、III区相关, II a区淋巴结转移与I b、II b、III、Va、Vc区相关, II b区淋巴结转移与II a、III、IV a、Va、Vb、VII a区相关, III区淋巴结转移与II a、II b、IV a、Va、Vb、Vc、VII a区相关, IV a区淋巴结转移与II a、II b、III、IV b、Va、Vc区相关, IV b区淋巴结转移与IV a区相关, Va区淋巴结转移与II b、III、IV a、Vb区、V区后缘间隙 (posterior to level V, PLV) 相关, Vb区淋巴结转移与III、Va、Vc区、PLV相关, Vc区淋巴结转移与II a、III、IV a、Vb区、PLV相关, VII a区淋巴结转移与II b、III区相关, PLV淋巴结转移与Va、Vb、Vc区相关 (P 均 <0.05)。**结论:** 鼻咽癌颈部淋巴结转移建立在上一站淋巴结转移的基础之上, 基于颈部各区淋巴结转移相关性的靶区勾画可以减少中危CTV的照射范围。

[关键词] 鼻咽癌; 颈部分区; 淋巴结转移; 相关性分析

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Correlation analysis of neck node levels in 709 cases of nasopharyngeal carcinoma JIANG Chaoyang¹, WANG Juan², ZHANG Ling¹, GAO Hui¹, ZHANG Tao¹, LI Zhihui¹ (1. Department of Oncology, the General Hospital of Western Theater Command, Chengdu 610083, Sichuan Province, China; 2. Department of Nuclear Medicine, the General Hospital of Western Theater Command, Chengdu 610083, Sichuan Province, China)

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[Abstract] **Background and purpose:** The research on radiotherapy clinical target volume (CTV) delineation based on the correlation analysis between neck node levels of nasopharyngeal carcinoma has not been reported. We retrospectively analyzed 709 cases of nasopharyngeal carcinoma with cervical lymph node metastasis, and aimed to provide a preliminary opinion for the CTV delineation of nasopharyngeal carcinoma based on the correlation analysis of node involvement in each neck node level. **Methods:** Based on the 2013 updated guideline of delineation of the neck node levels for head and neck tumors, we analyzed 709 nasopharyngeal carcinoma patients with cervical lymph node metastasis in the General Hospital of Western Theater Command from December 2011 to June 2018. The correlations between different levels were studied using χ^2 test and logistic regression model. **Results:** The top four node levels with the highest probability of metastasis were level II b (82.79%), level VII a (82.65%), level II a (60.50%) and level III (43.86%). Correlation analysis showed the lymph node metastasis in level I b was correlated with level II a and III, level II a was correlated with level I b, II b, III, Va and Vc, level II b was correlated with level II a, III, IV a, Va, Vb and VII a, level III was correlated with level II a, II b, IV a, Va, Vb, Vc and VII a, level IV a was correlated with level II a, II b, III, IV b, Va and Vc, level IV b was correlated with level IV a, level Va was correlated with level II b, III, IV a, Vb and posterior to level V (PLV), level Vb was correlated with level III, Va, Vc and PLV, level Vc was correlated with level II a, III, IV a, Vb and PLV, level

VIIa was correlated with level II b and III, and the PLV region was correlated with level Va, Vb and Vc (all $P < 0.05$). **Conclusion:** The lower cervical node involvement is based on the lymph node metastasis of upper levels. The delineation of intermediate risk CTV can be reduced based on the correlation analysis of neck node levels.

[Key words] Nasopharyngeal carcinoma; Neck node levels; Lymph node metastasis; Correlation analysis

鼻咽癌属于头颈部恶性肿瘤, 约80%的鼻咽癌患者发生在广东、广西及湖南等中国南部各省份^[1]。鼻咽癌颈部淋巴结转移率高达80%, 不仅影响鼻咽癌的临床分期, 也是预后的主要影响因素之一^[2-3]。2013年新版《头颈部肿瘤颈部淋巴结分区指南》^[4] (简称2013分区) 对进一步规范头颈部肿瘤放疗靶区的勾画具有重要意义, 但其对V区后缘间隙 (posterior to level V, PLV) 即斜方肌与肩胛提肌之间的间隙未做任何描述。有研究^[5-8]显示, 鼻咽癌患者颈部淋巴结跳跃性转移率为0.9%~1.6%, 这也反映出鼻咽癌颈部各区淋巴结转移可能具有相关性, 而基于2013分区的鼻咽癌颈部各区淋巴结转移相关性的研究尚未见报道。本研究旨在分析709例鼻咽癌患者颈部各区淋巴结转移间的相关性, 为鼻咽癌基于颈部各区淋巴结转移相关性的放疗靶区勾画提出初步意见。

1 资料和方法

1.1 临床资料

回顾性分析西部战区总医院709例经病理学检查确诊并伴有颈部淋巴结转移的鼻咽癌患者的资料 (表1), 男性509例, 女性200例, 中位年龄为50岁 (12~85岁)。病理学类型参照世界卫生组织 (World Health Organization, WHO) 肿瘤分型标准, 所有患者均按照《中国鼻咽癌分期2017版 (2008鼻咽癌分期修订专家共识)》进行重新分期^[9]。

1.2 颈部淋巴结分区标准

采用Grégoire等^[4]制定的2013分区。

1.3 颈部转移淋巴结的判定标准

所有患者均行CT定位及增强MRI检查, 颈部转移淋巴结的判定标准如下^[10]: ① 最大横断面图像上淋巴结最小径 ≥ 10 mm; ② 任何大小的淋巴结出现中央坏死或边缘环形强化或包膜外侵犯; ③ 同一高危区域淋巴结数量 ≥ 3 个, 每个淋

巴结最小径为8~10 mm; ④ 咽后淋巴结最大横断面的最小径 ≥ 5 mm; ⑤ 化疗或放疗后淋巴结明显缩小或消失。

表1 患者基线特征

Tab. 1 Patient baseline characteristics

Characteristic	Number of patients	[n (%)]
Gender		
Male	509	(71.79)
Female	200	(28.21)
Age/year		
<45	246	(34.70)
≥ 45	463	(65.30)
Histology		
WHO I	14	(1.97)
WHO II-III	695	(98.03)
T stage		
T ₁	189	(26.66)
T ₂	141	(19.89)
T ₃	195	(27.50)
T ₄	184	(25.95)
N stage		
N ₁	250	(35.26)
N ₂	352	(49.65)
N ₃	107	(15.09)
TNM stage		
II	124	(17.49)
III	305	(43.02)
IVa	267	(37.66)
IVb	13	(1.83)

1.4 统计学处理

采用SPSS 20.0对数据进行统计分析，各组淋巴结区的单因素分析采用 χ^2 检验（必要时采用Fisher精确检验），将 $P < 0.05$ 的因素纳入多因素分析，多因素分析采用logistic回归分析（选取进入法），为阐明logistic模型的拟合优度，同时进行Hosmer-Lemeshow检验，Hosmer-Lemeshow检验的 $P > 0.05$ 表明logistic模型具有良好的评估能力。多因素分析中 $P < 0.05$ 表示各区淋巴结转移间具有相关性。

2 结 果

2.1 颈部淋巴结转移情况

转移概率最高的前4位淋巴结区依次是：II b（82.79%）、VII a（82.65%）、II a（60.50%）、III区（43.86%）（图1，表2）。转移率低于5%的淋巴结区包括：I b(4.79%)、IV b（2.53%）、V c（1.26%）、PLV（4.37%）、VII b（0.84%）、VIII区（0.84%）。I a、VI、IX、X区均未见淋巴结转移。

2.2 各区淋巴结转移间的相关性分析

相关性分析结果显示，I b区淋巴结转移与II a、III区相关，II a区淋巴结转移与I b、II b、III、Va、Vc区相关，II b区淋巴结转移与II a、III、IVa、Va、Vb、VIIa区相关，III区淋巴结转移与II a、II b、IVa、Va、Vb、Vc、VIIa区相关，IVa区淋巴结转移与II a、II b、III、IVb、Va、Vc区相关，IVb区淋巴结转移与IVa区相关，Va区淋巴结转移与II b、III、IVa、Vb区、PLV相关，Vb区淋巴结转移与III、Va、Vc区、PLV相关，Vc区淋巴结转移与II a、III、IVa、Vb区、PLV相关，VIIa区淋巴结转移与II b、III区相关，PLV淋巴结转移与Va、Vb、Vc区相关，以上所有多因素分析的 P 均 < 0.05 ，VIIb区淋巴结转移与其余各淋巴结区间无相关性，各相关性结果见表3。

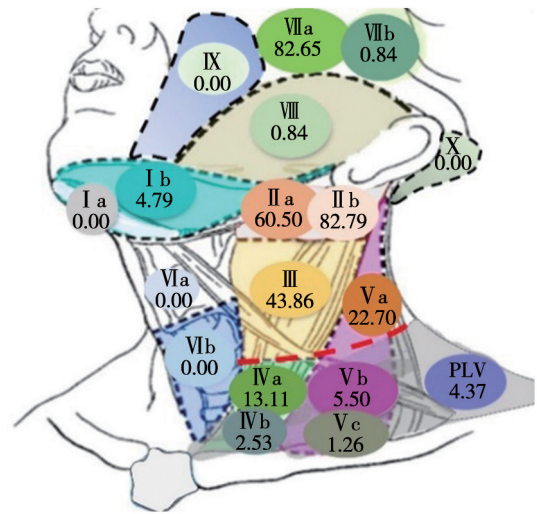


图1 各区淋巴结转移分布情况

Fig. 1 Distribution of lymph node metastasis in cervical levels

The red dotted line represents the cricoid cartilage layer

表2 鼻咽癌颈部各区淋巴结转移情况

Tab. 2 Patterns of cervical nodal metastasis of nasopharyngeal carcinoma

Neck node level	Number of patients [n (%)]
I a	0 (0.00)
I b	34 (4.79)
II a	429 (60.50)
II b	587 (82.79)
III	311 (43.86)
IV a	93 (13.11)
IV b	18 (2.53)
V a	161 (22.70)
V b	39 (5.50)
V c	9 (1.26)
PLV	31 (4.37)
VI	0 (0.00)
VII a	586 (82.65)
VII b	6 (0.84)
VIII	6 (0.84)
IX	0 (0.00)
X	0 (0.00)

表 3 颈部各淋巴结分区间的多因素分析 (P值)

Tab. 3 Multivariate analysis of cervical lymph node levels (P value)

Dependent variable	Covariates											
	I b	II a	II b	III	IV a	IV b	V a	V b	V c	VII a	VII b	PLV
I b	-	0.012	-	0.016	0.274	-	0.922	0.468	-	-	-	-
II a	0.007	-	0.001	0.002	0.055	0.246	0.048	0.199	0.006	-	-	0.470
II b	-	0.001	-	0.001	0.001	-	0.001	0.039	-	0.008	-	0.120
III	0.135	0.001	0.001	-	0.001	0.860	0.001	0.001	0.001	0.026	-	0.564
IV a	0.210	0.016	0.001	0.001	-	0.001	0.009	0.212	0.001	-	-	0.053
IV b	-	0.354	-	0.666	0.001	-	0.838	0.135	0.170	-	-	0.889
V a	0.902	0.057	0.001	0.001	0.009	0.825	-	0.001	0.090	0.273	-	0.001
V b	0.345	0.219	0.122	0.001	0.172	0.086	0.001	-	0.002	-	-	0.010
V c	-	0.004	-	0.009	0.004	0.234	0.086	0.004	-	-	-	0.011
VII a	-	-	0.003	0.004	-	-	0.122	-	-	-	-	-
VII b	-	-	-	-	-	-	-	-	-	-	-	-
PLV	-	0.552	0.690	0.730	0.560	0.715	0.001	0.005	0.032	-	-	-

-: No statistical significance in univariate analysis

3 讨 论

鼻咽癌易伴有颈部淋巴结转移, 约40%的鼻咽癌患者因颈部淋巴结肿大而就诊, 60%~90%的初诊患者存在淋巴结转移^[8, 11-12]。Wang等^[13]报道了3 100例鼻咽癌患者基于2013分区的颈部淋巴结转移情况, 淋巴结转移最高的前4位依次是: II b (84.56%)、VII a (79.35%)、II a (65.17%)、III区 (45.06%), 与本研究结果一致, 提示II b与VII a区可能均为鼻咽癌淋巴结转移的第1站, 同时该报道也指出2013分区中的V区后界未能充分地覆盖PLV。本研究观察到有31例 (4.37%) 患者PLV淋巴结转移, 一并纳入到淋巴结转移的相关性分析中。有研究^[5-8]显示, 鼻咽癌颈部淋巴结转移规律性较强, 即按照从上到下同侧循序的规律逐站转移, 淋巴结跳跃性转移的概率为0.9%~1.6%, 间接反映了鼻咽癌颈部各区淋巴结转移具有相关性, 这也是开展本研究的前提。本研究的相关性分析再次说明鼻咽癌颈部淋巴结转移规律性较强, 下一站淋巴结转移建立在上一站淋巴结转移的基础之上, 同时本研究发

现, 无论鼻咽癌颈部淋巴结转移发生在单侧或双侧, 都符合上述转移规律。淋巴结受累支持颈部常规照射, 鼻咽癌颈部淋巴结CTV通常包括双侧咽后淋巴结区域及II~V淋巴引流区, 在过去的10年中, 一些研究者已经发表或更新了颈部淋巴结CTV的勾画建议^[14-19], 最近的更新为2013分区^[4], 但该指南中建议的勾画界限仅适用于淋巴结阴性患者, 而本研究在淋巴结阳性患者的基础上进行, 此外国际鼻咽癌勾画指南建议所有的T和N分期患者均应将双侧咽后淋巴结区及II、III、V a区包括在中危CTV内, 如果同侧颈部有除咽后淋巴结外的任何淋巴结转移, 中危CTV均应该包括IV、V b区, 另外当同侧颈部没有淋巴结转移时IV、V b区可以免除照射^[19]。

基于调强放疗的靶区勾画已使鼻咽癌患者的预后得到很大提升^[1, 20], 但不同鼻咽癌患者淋巴结转移区域不同, 更加个体化的靶区勾画原则及如何进一步降低放疗不良反应仍值得探索。本研究中共18例 (2.53%) 患者伴有IV b区淋巴结转移, 多因素分析显示, IV b区淋巴结转移仅与IV a区相关, 18例IV b区淋巴结转移者均同时伴有IV a

区淋巴结转移。共161例(22.70%)患者伴有Va区淋巴结转移,多因素分析显示,Va区淋巴结转移与IIb、III、IVa、Vb区、PLV相关,但与VIIa、IIa区无关。161例Va区淋巴结转移并同时伴有IIb、III、IVa、Vb区、PLV淋巴结转移的患者分别为161、136、63、37、31例。进一步分析显示,共40例患者伴有IIa区而无IIb区淋巴结转移,这40例患者中无1例出现Va区淋巴结转移。此外,在586例VIIa区淋巴结转移的患者中,有444例患者不伴有Va区淋巴结转移。本研究中未见1例仅VIIa及Va区出现淋巴结转移的患者。基于本研究笔者提出鼻咽癌颈部中危CTV勾画的初步概念,即将颈部中危CTV定义为与本组淋巴结转移相关的同侧颈部淋巴结区(图2),而将非相关淋巴结区选择性定义为低危CTV,两者给予不同的放疗剂量。Ib区的靶区勾画仍需参照现有指南^[19],关于PLV的靶区勾画笔者前期已做报道^[11]。与现有指南相比,本研究减少了中危CTV的照射范围^[19]。



图2 各区淋巴结转移所对应的同侧中危CTV

Fig. 2 The ipsilateral cervical lymph node levels and related intermediate risk CTV

The left columns represent the metastatic lymph node levels, the right columns represent the intermediate risk CTVs which should be delineated

本研究不足之处在于:①Vc区转移患者少,统计分析存在偏倚,其准确性较差,VIII区淋巴结转移患者为6例,且均表现为同侧颈部淋巴结明显肿大产生局部压迫,考虑VIII区淋巴结转移多系淋巴回流受阻从而导致反流,因此未纳入统计分析中。②本研究针对达到转移淋巴结诊断标准的患者,没有充分考虑到尚未达到淋巴结诊断标准的颈部淋巴结肿大患者。③本研究亦未能充分考虑到淋巴结包膜外侵犯及淋巴结跳跃性转移的情况。④本研究未纳入N₀期鼻咽癌患者。

综上所述,关于鼻咽癌颈部各区淋巴结转移相关性的放疗靶区勾画未见报道,本研究首次对基于2013分区的鼻咽癌颈部各区淋巴结转移相关性的放疗靶区勾画提出初步意见,体现了鼻咽癌放疗靶区勾画的个体化原则,但鼻咽癌患者颈部淋巴结转移率高,而因放疗靶区勾画不足导致颈部淋巴结复发将极大地影响患者预后,因此本研究的结论仍有待更大样本量试验的验证及前瞻性临床研究的探索。

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