

基于2013版颈部淋巴结分区指南的 鼻咽癌淋巴结转移规律与预后价值研究

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[摘要] 背景与目的: 2013年欧洲肿瘤学会官方杂志*Radiotherapy & Oncology*发表了新版头颈部肿瘤颈部淋巴结分区指南, 对规范颈部淋巴结靶区的勾画有重要意义。该研究采用2013版颈部淋巴结分区指南, 旨在探讨鼻咽癌颈部淋巴结转移规律, 以及颈部淋巴结影像特征与预后的关系, 为将来修订N分期提供依据。**方法:** 回顾性分析本院2009年1月—2010年12月病理诊断明确的、初诊无远处转移、接受调强放射治疗的鼻咽癌患者656例。所有患者治疗前行鼻咽和颈部MRI扫描。回顾分析所有患者的MRI图像, 并根据2013版颈部淋巴结分区指南进行重新分区, 分析颈部淋巴结转移的影像学特征与预后的关系。**结果:** 中位随访时间为46.9个月。4年无局部复发生存率为91.3%, 4年无颈部复发生存率为95.1%, 4年无远处转移生存率为87.7%, 4年无病生存率为78.5%, 4年总生存率为92.8%。最常见的颈部淋巴结转移分区为: II区76.2%, VIIa区65.1%, 其次为III区(50.4%), Va(17.5%)和IVa(11.7%)。淋巴结的跳跃转移率为1.0%。颈部淋巴结阳性的患者中, 46.4%的患者有淋巴结坏死, 74.4%的患者有包膜外侵犯。单因素分析显示, 颈部淋巴结受累侧数、颈部淋巴结最大径 ≥ 6 cm、颈部淋巴结坏死、T分期和N分期都是影响无远处转移生存和无病生存的因素($P < 0.05$)。淋巴结包膜外侵犯有影响无远处转移生存率的趋势($P = 0.060$)。环状软骨下缘以下的颈部分区受累对无远处转移生存和无病生存无显著影响。多因素分析发现, T分期、淋巴结最大径是影响无远处转移生存的独立预后因素($P < 0.05$); T分期、淋巴结最大径和淋巴结坏死是影响无病生存的独立预后因素($P < 0.05$)。**结论:** 该研究阐明了鼻咽癌颈部淋巴结转移规律, 发现颈部淋巴结受累侧数、淋巴结最大径、淋巴结坏死是影响远处转移和无病生存的重要因素。下颈部受累对无远处转移生存和无病生存无显著影响。

[关键词] 鼻咽癌; 颈部淋巴结转移规律; 淋巴结坏死; 包膜外侵犯; 远处转移

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[Abstract] **Background and purpose:** In 2013, the official journal of European Society of Radiotherapy & Oncology (ESTRO) - *Radiotherapy & Oncology* published the updated version of Consensus Guidelines of Delineation of the neck node levels for head and neck tumors, which contributed to the standardization of description of neck nodal metastasis, as well as reduction of treatment variations from various institutions. This study applied this updated guidelines to analyze the patterns of lymph node metastasis of nasopharyngeal carcinoma and explore the prognostic value of the radiologic characteristics of nodes, in order to provide evidence for future revision of N staging system. **Methods:** A total of 656 patients from Jan. 2009 to Dec. 2010 were retrospectively recruited to analysis. All were pathologically diagnosed as non-metastatic nasopharyngeal carcinoma, treated with intensity-modulated radiotherapy. All patients received a pretreatment MRI scan. We retrospectively reviewed the MRI imaging of 656 patients and

mapped the lymph node metastasis using the 2013 International Consensus Guidelines. **Results:** Median follow-up was 46.9 months. Four-year local recurrence-free survival, nodal recurrence-free survival, distant metastasis-free survival, disease-free survival and overall survival was 91.3%, 95.1%, 87.7%, 78.5% and 92.8%, respectively. The most common metastatic node levels were level II (76.2%) and level VIIa (65.1%), followed by level III (50.4%), Va(17.5%) and IVa (11.7%). There was a very low incidence of node skipping (1.0%). Cervical nodal necrosis was observed in 46.4% of patients with positive nodes and extracapsular spread was noted in 74.4% of them. Univariate analysis showed that bilateral nodal involvement, greatest dimension of positive nodes (≥ 6 cm), central nodal necrosis, T stage and N stage were prognostic factors for disease-free survival and distant metastasis-free survival ($P < 0.05$). Extracapsular spread showed a trend to correlate with poor distant metastasis-free survival ($P = 0.060$). The involvement of lower neck levels (below the caudal border of cricoid cartilage) did not have a significant impact on disease-free survival and distant metastasis-free survival. In multivariate analysis, T stage and greatest dimension of nodes (≥ 6 cm) were independent prognostic factors for distant metastasis-free survival ($P < 0.05$). T stage, greatest dimension of nodes (≥ 6 cm) and central nodal necrosis were independent prognostic factors of disease-free survival ($P < 0.05$). **Conclusion:** This study demonstrates the patterns of lymph node metastasis of nasopharyngeal carcinoma based on 2013 International Consensus Guidelines. Bilateral nodal involvement, greatest dimension of positive nodes and central nodal necrosis had prognostic values on disease-free survival and distant metastasis-free survival. In our study, the involvement of lower neck levels was not proved to be a prognostic factor for disease-free survival and distant metastasis-free survival.

[**Key words**] Nasopharyngeal carcinoma; Pattern of cervical nodal metastasis; Nodal necrosis; Extracapsular spread; Metastasis

鼻咽癌的颈部淋巴结转移非常常见, 文献报道85%的鼻咽癌有颈部淋巴结转移^[1]。充分了解鼻咽癌淋巴结的转移规律, 对于诊断、分期、制定治疗计划十分重要。尤其是在调强放射治疗广泛应用的今天, 如何准确勾画淋巴结引流区的靶区, 尽量避免靶区范围不足而导致的剂量不足, 以及靶区范围过大导致正常组织剂量偏高, 对提高局控、改善生活质量都十分重要。基于这一出发点, 欧洲放射肿瘤协会(European Society of Radiotherapy & Oncology, ESTRO)和肿瘤放射治疗协助组(Radiation Therapy Oncology Group, RTOG)等多个协作小组经过充分的协商, 在2003版颈部淋巴结分区指南^[2]和TNM颈部淋巴结分区^[3]的基础上, 提出了2013版头颈部肿瘤颈部淋巴结分区指南(简称2013版颈部淋巴结分区指南)^[4]。该指南在原来Robbins分区的6个亚区的基础上, 演变为10个分区, 新增了锁骨上内侧组(IVb)、锁骨上外侧组(Vc)、茎突后淋巴结组(VIIb)、腮腺淋巴结组(VIII)、面颊淋巴结组(XI)和后颅淋巴结组(X, 包括耳后和枕部淋巴结), 并对原来分区描述更为细化。目前, 基于2013版颈部淋巴结分区指南描述鼻咽癌颈部淋巴结转移规律的文

献尚较少^[5-6], 尤其是包括临床随访资料的颈部淋巴结分区的研究比较缺乏, 目前只有Yue等^[5]报道了基于新分区指南的鼻咽癌颈部淋巴结分区指南和预后的关系。为探讨基于新分区指南的鼻咽癌颈部淋巴结转移规律, 明确颈部淋巴结转移影像学特征与临床预后的关系。本研究通过回顾性分析656例鼻咽癌患者的临床和影像学资料, 分析基于2013版颈部淋巴结分区指南的鼻咽癌淋巴结转移情况、影像学特征和预后的关系。

1 材料和方法

1.1 患者临床特征

回顾性分析2009年1月—2010年12月在复旦大学附属肿瘤医院病理诊断明确、无远处转移的初诊鼻咽癌患者656例。其中男性485例, 女性171例, 平均年龄为49岁, 95.3%病理类型为WHO II ~ III型, 0.3%的病理类型为WHO I型, 其余为其他病理类型。所有患者治疗前接受完整的体格检查、间接鼻咽镜检查或纤维鼻咽镜检查, 鼻咽和颈部MRI增强、胸部CT、腹部B超、骨扫描或正电子放射断层扫描(positron emission tomography/computed tomography,

PET/CT)检查。所有患者采用AJCC(American Joint Committee on Cancer)分期第六版进行初始分期和决定治疗策略。

1.2 图像分析

所有患者行鼻咽和颈部MRI检查(GE公司, 1.5T), 采用头颈线圈, 扫描范围为: 眼眶上缘至胸锁关节下缘。一位高年资放射诊断学医师和一位高年资放射肿瘤治疗学医师重新核片, 并根据2013版颈部淋巴结分区指南进行重新分区。所有读片不一致处均通过讨论协商解决。诊断颈部淋巴结转移的标准为: ①任何咽后淋巴结外侧组横断面上最小径 ≥ 5 mm, 或任何可见的内侧组咽后淋巴结, 或颈静脉二腹肌区淋巴结(II A区)横断面最小径 ≥ 11 mm, 或其他颈部淋巴结横断面最小径 ≥ 10 mm; ②颈部淋巴结有环形强化, 或中央坏死, 无论大小; ③同一高危区域有3个以上淋巴结, 其中一个最大横断面的最小径 ≥ 8 mm^[7]; ④颈部淋巴结有包膜外侵犯, 无论大小^[8]。所有患者按照2010年AJCC分期进行重新分期。

1.3 治疗策略

所有患者依据复旦大学附属肿瘤医院当时的诊疗指南进行治疗, 对I~II_A期患者推荐单纯放疗, 对II_B期患者推荐同期放化疗, 对III、IV_A、IV_B期患者推荐放化疗综合治疗, 包括诱导化疗+同期放化疗/放疗, 同期放化疗以及同期放化疗+辅助化疗。总体而言, 85.8%的患者接受了以顺铂为基础的化疗。所有患者接受调强放射治疗, 具体剂量为: T₁~T₂原发灶66 Gy/30 f(2.2 Gy/f); T₃~T₄原发灶70.4 Gy/32f(2.2 Gy/f); 颈部阳性淋巴结66 Gy/(30~32) f, 亚临床病灶及颈部高危区60 Gy/(30~32) f, 颈部低危区54 Gy/(30~32) f。调强放射治疗的细节详见之前的报道^[9]。若放疗后鼻咽腔内或颈部病灶残留, 可酌情给予腔内后装治疗或电子线加量治疗。

1.4 随访策略

治疗结束后第1~2年, 所有患者至少每3个月进行随访1次, 治疗结束后2~5年, 每半年

随访1次直至失访或死亡。随访内容包括: 完整的体格检查、间接鼻咽镜检查或纤维鼻咽镜检查, 鼻咽和颈部MRI增强、胸部CT、腹部B超, 必要时行骨扫描或PET/CT检查。

1.5 统计学处理

所有患者从放疗结束日起随访至死亡、或失访。分别统计总生存(overall survival, OS)、无局部复发生存(local recurrence-free survival, LRFS)、无颈部复发生存(nodal recurrence-free survival, DMFS)和无远处转移生存(distant metastasis-free survival, DFS)。用SPSS 16.0统计软件进行统计分析, Kaplan-Merier法计算生存率, Log rank法进行不同因素间生存率的比较。Cox风险模型进行多因素分析。

2 结 果

所有患者按照2010年AJCC分期进行重新分期, T分期分别为: T₁为33.1%(217/656), T₂为33.5%(220/656), T₃为21.8%(143/656), T₄为11.6%(76/656); N分期分别为: N₀为14.2%(93/656), N₁为46.8%(307/656), N₂为25.5%(167/656), N₃为13.6%(89/656); I期、II期、III期、IV_A期和IV_B期分别为7.0%(46/656)、33.7%(221/656)、35.2%(231/656)、10.5%(69/656)和13.6%(89/656)。中位随访时间为46.9个月。所有患者4年无局部复发生存率为91.3%, 4年无颈部复发生存率为95.1%, 4年无远处转移生存率为87.7%, 4年无病生存率为78.5%, 4年总生存率为92.8%。

2.1 淋巴结转移规律

按照2013版颈部淋巴结分区指南, 鼻咽癌各淋巴结分区的转移规律见表1。最常见的颈部淋巴结转移分区为: II区76.2%, VIIa区65.1%, 其次为III区(50.4%), Va(17.5%)和IVa(11.7%)。Ib、IVb、Vb、Vc、VIIb和VIII的淋巴结转移概率低于5.0%。Ia区、VI区、XI区和X区未见淋巴结转移。

在2013版颈部淋巴结分区指南新增的颈部

分区中, 茎突后间隙(VIIb区)受累的有4例患者(图1), 这4例均有II区和咽后淋巴结受累, 以及II区淋巴结包膜外侵, II区淋巴结最大径均 >2 cm。在腮腺淋巴结转移(VIII区)的10例患者中(图2), 10例有II区淋巴结转移, 9例有III区淋巴结受累, 并且6例II区淋巴结表现为包膜外侵犯、淋巴结融合, II区淋巴结平均最大径为2.68 cm。IVb区受累的16例患者中, 全部有IVa区淋巴结转移, 3例有Vb区淋巴结转移。Vc区受累的6例患者全部均有Vb区淋巴结转移。我们进一步分析淋巴结跳跃转移的情况。II区无转移而III区转移者2例, Va区无转移而Vb区转移者3例, 总的跳跃转移率为1.0%(5/507)。

表 1 鼻咽癌颈部淋巴结转移规律

Tab. 1 Patterns of cervical nodal metastasis of nasopharyngeal carcinoma

Neck node level	Number	Percentage/%
I a	0	0.0
I b	17	2.6
II	500	76.2
II a	258	39.3
II b	412	62.8
III	331	50.4
IVa	77	11.7
IVb	16	2.4
Va	115	17.5
Vb	13	2.0
Vc	6	0.9
VI	0	0.0
VIIa	427	65.1
VIIb	4	0.6
VIII	10	1.5
IX	0	0.0
X	0	0.0

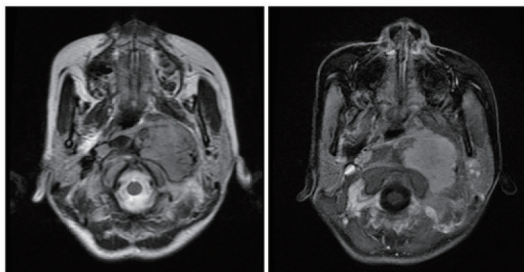


图 1 左侧茎突后淋巴结受累鼻咽癌患者的横断面T2WI(左)和T1WI增强(右)序列MRI图像

Fig. 1 The axial T2WI (left) and T1WI contrast (right) MR images of a patient with nasopharyngeal carcinoma who presented with involvement of left retro-styloid nodes

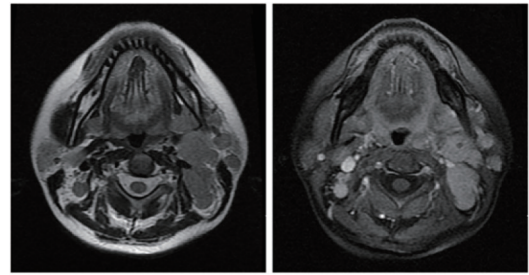


图 2 左侧腮腺淋巴结受累的鼻咽癌患者的横断面T2WI(左)和T1WI增强(右)序列MRI图像

Fig. 2 The axial T2WI (left) and T1WI contrast (right) MR images of a patient with nasopharyngeal carcinoma who presented with involvement of left parotid nodes

2.2 单因素分析

在507例颈部淋巴结阳性(不含咽后淋巴结)患者中, 颈部淋巴结最大径为 (37.4 ± 18.0) mm, 65例(12.8%)颈部淋巴结最大径 ≥ 60 mm。57.2%(290/507)的患者表现为单侧颈部受累, 42.8%(217/507)的患者双侧颈部受累。46.4%(235/507)的患者有淋巴结坏死, 74.4%(377/507)有包膜外侵。临床体检发现锁骨上窝受累者有43例(6.6%), 影像学检查发现环状软骨下缘以下的下颈部受累者(IVa、IVb、Vb、Vc区)有83例(12.7%)。

单因素分析显示, 颈部淋巴结受累侧数、颈部淋巴结最大径 ≥ 6 cm、颈部淋巴结坏死都是影响无远处转移生存的因素($P=0.014$ 、 0.010 、 0.032 , 表2和图3~5)。T分期和N分期也是影响无远处转移生存的因素($P=0.001$ 、 0.015)。淋巴结包膜外侵犯有影响无远处转移率的趋势($P=0.060$)。环状软骨下缘以下的颈部分区受累对无远处转移生存和无病生存无显著影响($P=0.306$, 图6)。同样, 颈部淋巴结受累侧数、颈部淋巴结最大径 ≥ 6 cm、颈部淋巴结坏死也是影响无病生存的因素($P=0.016$ 、 0.002 、 0.000 , 表2), T分期和N分期亦是影响无病生存的因素($P=0.001$ 、 0.012)。

2.3 多因素分析

我们把一系列临床和影像学特征纳入多因素分析。若把年龄、T分期、颈部淋巴结受累侧

数、淋巴结坏死、淋巴结最大径和临床体检的锁骨上窝受累纳入分析,则T分期、淋巴结最大径是影响无远处转移的独立预后因素($P<0.05$),淋巴结受累侧数临界有意义($P=0.055$,表3,左列)。若以影像学检查的下颈部受累(IVa、IVb、Vb和Vc受累)替代锁骨上窝受累纳入多因素分

析,则T分期、淋巴结最大径是影响无远处转移的独立预后因素($P<0.05$),淋巴结受累侧数临界有意义($P=0.058$,表3,右列)。同样,若把上述临床和影像学纳入多因素分析,则T分期、淋巴结最大径和淋巴结坏死是影响无病生存的独立预后因素($P<0.05$,表4)。

表 2 鼻咽癌颈部淋巴结临床影像特征与无远处转移、无病生存的关系(单因素分析)

Tab. 2 Univariate analysis of various clinical and radiologic factors of neck node metastasis of nasopharyngeal carcinoma on distant metastasis-free survival and disease-free survival

Factors	DMFS (<i>P</i> value)	DFS (<i>P</i> value)
Bilateral nodal involvement	0.014*	0.016*
The maximum dimension of nodes ≥ 6 cm	0.010*	0.002*
The maximum dimension of nodes ≥ 3 cm	0.204	0.070
Central nodal necrosis	0.032*	0.000*
Extracapsular spread	0.060	0.091
The involvement of lower neck levels (IVa, IVb, Vb, Vc)	0.306	0.125
The involvement of the supraclavicular fossa (Ho's triangle by physical examination)	0.764	0.840

*: $P<0.05$. DMFS: Distant metastasis-free survival; DFS: Disease-free survival.

表 3 鼻咽癌颈部淋巴结临床影像特征与无远处转移生存的关系(多因素分析)

Tab. 3 Multivariate analysis of various clinical and radiologic factors of neck node metastasis of nasopharyngeal carcinoma on distant metastasis-free survival

Analysis of various factors including the involvement of supraclavicular fossa			Analysis of various factors including the involvement of lower neck levels (IVa, IVb, Vb, Vc)		
Factor	<i>P</i> value	HR (95%CI)	Factor	<i>P</i> value	HR (95%CI)
Age	0.529	1.006(0.986-1.027)	Age	0.618	1.005(0.985-1.025)
T stage	0.001*	1.505(1.172-1.933)	T stage	0.001*	1.515(1.178-1.948)
Bilateral nodal involvement	0.055	1.657(0.990-2.773)	Bilateral nodal involvement	0.058	1.649(0.983-2.767)
Maximum dimension of nodes ≥ 6 cm	0.020*	2.133(1.125-4.041)	Maximum dimension of nodes ≥ 6 cm	0.039*	2.109(1.037-4.292)
Central nodal necrosis	0.334	1.298(0.764-2.205)	Central nodal necrosis	0.336	1.297(0.764-2.202)
Involvement of supraclavicular fossa	0.332	0.853(0.619-1.175)	Involvement of lower neck levels	0.638	0.841(0.408-1.732)

*: $P<0.05$.

表 4 鼻咽癌颈部淋巴结临床影像特征与无病生存的关系(多因素分析)

Tab. 4 Multivariate analysis of various clinical and radiologic factors of neck node metastasis of nasopharyngeal carcinoma on disease-free survival

Analysis of various factors including the involvement of supraclavicular fossa			Analysis of various factors including the involvement of lower neck levels (IVa, IVb, Vb, Vc)		
Factor	<i>P</i> value	HR(95%CI)	Factor	<i>P</i> value	HR(95%CI)
Age	0.478	1.006(0.990-1.021)	Age	0.582	1.004(0.989-1.020)
T stage	0.000*	1.413(1.166-1.714)	T stage	0.000*	1.421(1.171-1.724)
Bilateral nodal involvement	0.110	1.381(0.930-2.052)	Bilateral nodal involvement	0.125	1.366(0.917-2.032)
Maximum dimension of nodes ≥ 6 cm	0.010*	1.952(1.175-3.244)	Maximum dimension of nodes ≥ 6 cm	0.033*	1.829(1.049-3.188)
Central nodal necrosis	0.022*	1.619(1.072-2.445)	Central nodal necrosis	0.024*	1.608(1.065-2.428)
Involvement of supraclavicular fossa	0.267	0.872(0.685-1.110)	Involvement of lower neck levels	0.843	0.946(0.545-1.642)

*: $P<0.05$.

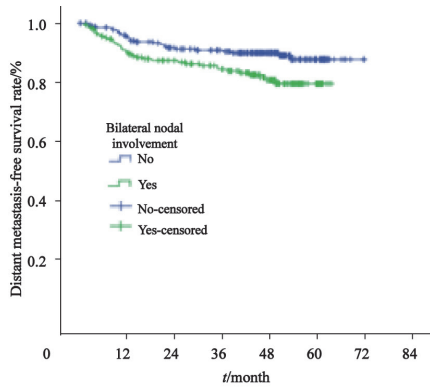


图3 单/双侧颈部淋巴结受累者的无远处转移生存情况

Fig.3 Distant metastasis-free survival stratified by bilateral nodal involvement

The 4-year distant metastasis-free survival of patients with bilateral nodal involvement was lower than that of unilateral nodal involvement (80.7% vs 89.9%, $P=0.014$).

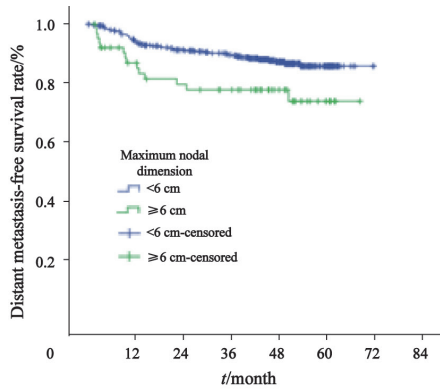


图4 不同颈部淋巴结最大径者的无远处转移生存情况

Fig.4 Distant metastasis-free survival stratified by the maximum nodal dimension

The 4-year distant metastasis-free survival of patients with maximum nodal dimension ≥ 6 cm was lower than that of maximum nodal dimension <6 cm (77.7% vs 87.2%, $P=0.010$).

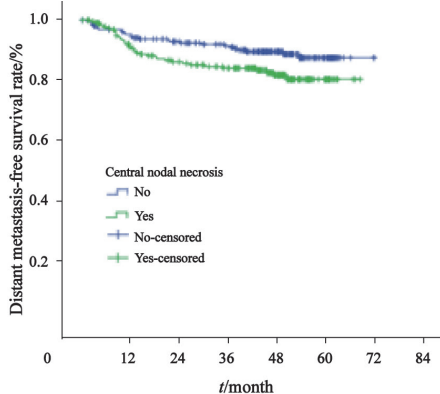


图5 有/无颈部淋巴结坏死者的无远处转移生存情况

Fig.5 Distant metastasis-free survival stratified by central nodal necrosis

The 4-year distant metastasis-free survival of patients with central nodal necrosis was lower than that without central nodal necrosis (81.7% vs 89.5%, $P=0.032$).

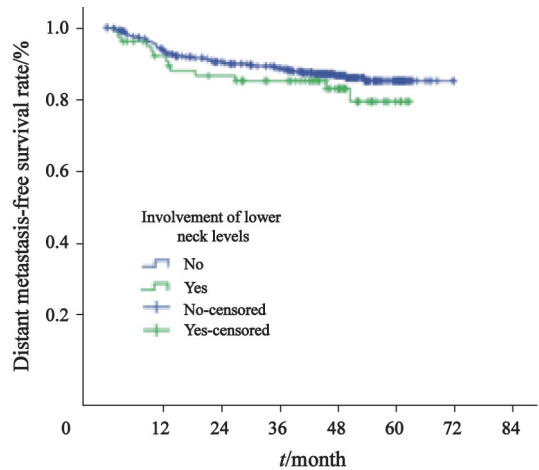


图6 有/无下颈部受累者(环状软骨下缘的颈部分区)的无远处转移生存情况

Fig.6 Distant metastasis-free survival stratified by the involvement of lower neck levels (below cricoid cartilage, including level IVa, IVb, Vb and Vc)

The 4-year distant metastasis-free survival were not statistically significant with and without involvement of lower neck levels (82.9% vs 86.6%, $P=0.306$).

3 讨论

本研究通过回顾性分析656例鼻咽癌患者的临床和影像学资料,运用2013版颈部淋巴结分区勾画指南对颈部转移淋巴结进行分区,有利于进一步了解鼻咽癌淋巴结转移的规律,有助于鼻咽癌颈部淋巴结引流区靶区勾画的规范化。本研究发现,最常见的颈部淋巴结引流区为II区76.2%,VIIa区65.1%。这与Ho等^[1]和Yue等^[5]及王孝深等^[10]学者的观察一致。II区淋巴结和咽后淋巴结是鼻咽癌的第一站淋巴结。除了II区和VIIa区,我们发现淋巴结转移风险较高的为III区(50.4%),IVa(11.7%)和Va(17.5%)区;而Ib、IVb、Vb、Vc、VIIb、VIII的淋巴结转移概率低于5.0%。这与Ho等的研究也一致。Ho等^[1]对411篇文献的鼻咽癌颈部淋巴结转移进行荟萃分析(基于2003版颈部淋巴结分区指南^[2]),发现最常见的淋巴结转移区为II区(70.4%)和咽后淋巴结区(69.4%),其次为III、V和IV区(44.9%、26.7%和11.2%),Ia、Ib、VI区、锁骨上窝和腮腺区转移的概率合计8.8%。相似地,Yue等^[5]也发现IIb区(59.6%)和VIIa区(75.4%)转移概率最高(基于2013版颈部

淋巴结分区指南^[4]), 其次是Ⅱa、Ⅲ、Ⅳa和Ⅴa区(36.8%、19.6%、4.6%和4.2%), 其他淋巴结分区转移概率低于2.0%。基于上述研究, 我们认为Ⅱ和Ⅶa区(即咽后淋巴结区)为鼻咽癌的第一站淋巴结, 其次Ⅲ、Ⅳa和Ⅴa区为第二站转移淋巴结。淋巴结转移大多遵循逐级转移, 跳跃性转移的概率很低, 本研究中跳跃性转移率为1.0%, Ho等^[1]报道跳跃性转移率在0.5%~7.9%之间^[1]。

本研究进一步分析了2013版颈部淋巴结勾画指南中新增的分区的转移特点, 发现腮腺淋巴结转移的患者大多合并Ⅱ、Ⅲ区的转移, 并且Ⅱ区淋巴结直径较大, 多伴有包膜外侵犯、融合, 这提示腮腺淋巴结的转移可能与Ⅱ区淋巴结的广泛受累、逆行转移有关。茎突后淋巴结转移的患者全部有Ⅱ区淋巴结的转移, 并且Ⅱ区淋巴结直径较大, 伴有包膜外侵犯和融合, 这提示茎突后间区的转移可能与Ⅱ区淋巴结广泛受累, 逆行转移有关, 这与2013版颈部淋巴结分区指南中专家意见也是一致^[4]。

颈部淋巴结的影像学特征包括: 受累侧数、最大长径、坏死、包膜外侵犯、受累分区等。颈部淋巴结的受累侧数与肿瘤负荷有关, Mao等^[11]和Yue等^[5]学者和我们的研究均发现颈部淋巴结受累侧数是影响无远处转移生存和无病生存的独立预后因素。关于淋巴结最大长径是否影响无远处转移, 以及合适的阈值为多少, 各家的报道略有不同。Mao等^[11]发现颈部淋巴结的分区, 而不是颈部淋巴结的直径, 是影响无远处转移生存和无病生存的独立预后因子。而Yue等^[5]的研究发现颈部淋巴结最大径(>6 cm)和何氏锁骨上窝受累都是影响无病生存和无远处转移生存的独立预后因素。Pan等^[12]学者则认为, 淋巴结最大径3 cm而不是6 cm作为阈值及N分期的标准, 更适合预测无远处转移生存。我们的研究则发现颈部淋巴结最大径(≥6 cm)是影响无远处转移生存和无病生存的独立预后因素。我们认为, 淋巴结大小与肿瘤负荷有关, 对于远处转移有重要的预测价值, 不可被淋巴结受累分区替代。鉴于上述研究, 我

们认为颈部淋巴结≥6 cm仍是鼻咽癌N分期的较好的标准之一。

颈部淋巴结坏死, 在MRI表现为局灶性的T2序列上高信号和T1序列低信号, 可伴有或不伴有环形增强^[13]。淋巴结坏死在头颈部鳞癌中十分常见, 是诊断淋巴结转移的十分可靠的标准^[7, 13]。淋巴结坏死的概率与淋巴结直径有关, 56%~63%的直径>1.5 cm的恶性淋巴结有坏死的征象, 而直径<1 cm的淋巴结只有10%~33%的概率表现为坏死^[14-15]。文献报道, MRI诊断颈部淋巴结坏死的灵敏度和特异度与CT相似, 其灵敏度、特异度、准确性分别为93%、89%、91%^[13]。鉴于此, 我们分析了颈部淋巴结坏死对无远处转移和无病生存的预后价值。我们发现, 颈部淋巴结坏死者有更差的无远处转移生存和无病生存, 并且在多因素分析中, 颈部淋巴结坏死是无病生存的独立预后因素。Lan等^[16]回顾性分析了1 800例鼻咽癌患者, 其中颈部淋巴结坏死率为44.0%, 这与我们报道的46.4%较为接近。并且颈部淋巴结坏死是总生存、无病生存、无颈部复发生存和无远处转移生存的独立预后因素。考虑到颈部淋巴结坏死诊断的灵敏度和特异度较高, 以及对无远处转移和无病生存的预测价值, 建议在鼻咽癌分期修订时考虑纳入颈部淋巴结坏死这一特征。

影像诊断包膜外侵犯的标准是淋巴结边缘模糊, 不规则的淋巴结包膜强化, 或浸润邻近脂肪或肌肉^[8]。在头颈部鳞癌的患者中, 包膜外侵犯与淋巴结大小密切相关。50%以上的2~3 cm的淋巴结或75%以上的>3 cm的淋巴结有包膜外侵犯。然而, 包膜外侵犯在小淋巴结中也十分常见。有报道称23%的<1 cm的阳性淋巴结也有包膜外侵犯^[17-18]。淋巴结包膜外侵犯, 不仅是诊断头颈部淋巴结转移的标准, 还影响预后和治疗^[19-20]。包膜外侵犯与局部复发、远处转移和不良预后有关^[19, 21]。在头颈部鳞癌中, 包膜外侵犯需要更大的颈清扫范围, 并且术后需行辅助放化疗^[22]。Mao等^[11]发现, 淋巴结包膜外侵犯是影响鼻咽癌无病生存和无

远处转移生存的独立预后因素。我们的研究发现淋巴结包膜外侵犯者似乎有更高的远处转移趋势($P=0.060$),但在多因素分析中,包膜外侵犯并未证实对无远处转移生存和无病生存有独立预后价值。这可能与诊断包膜外侵犯的灵敏度、特异度有关。文献报道,与术后病理对照,MRI诊断的颈部淋巴结包膜外侵犯的灵敏度、特异度与CT相似,其灵敏度、特异度和准确性分别为78%、86%和80%^[8]。由于其灵敏度、特异度较低,各观察者对诊断包膜外侵犯又存在一定的差异,我们认为暂不支持把包膜外侵犯纳入鼻咽癌N分期的标准中。

锁骨上窝概念最早是由何鸿超教授在1970年左右提出^[23],即这3点之间的三角形区域:锁骨胸骨端的上缘,锁骨外侧端的上缘和颈肩交界处,由于锁骨上窝的定义是基于临床体检,不同观察者间存在一定差异,后来学者提出应该以标准的颈部淋巴结分区替代锁骨上窝的概率。Ng等^[24]以Som等^[25]分区的IV和Vb区替代锁骨上窝,发现IV和Vb区受累是对无远处转移生存和总生存有预测价值。同样的,Li等^[26]报道,基于2003版EORTC分期^[2]的IV、Vb和锁骨上窝受累是无远处转移生存和无病生存的独立预后因素。Yue等^[5]学者应用2013版颈部淋巴结分区,也发现以环状软骨下缘的颈部受累(IVa, IVb, Vb, Vc),替代锁骨上窝的概念能使不同N分期的无远处转移曲线分布更为合理,下颈部受累是无病生存和无远处转移生存的独立预后因素。然而,在我们的研究中,临床锁骨上窝和环状软骨下缘的颈部受累在单因素和多因素分析中,未发现对无病生存和无远处转移生存有预测价值。我们认为,这可能由于两组的患者数较少,在507例颈部淋巴结阳性的患者中,仅有43例患者临床体检有锁骨上窝受累,83例患者有影像学的下颈部受累。其次,临床体检锁骨上窝受累可能存在不同观察者的差异。再者,何氏分期锁骨上窝的范围包括部分的IVa和Vb、全部IVb和Vc的范围,不等同于下颈部受累,我们认为IVa和Vb区受累与IVb和Vc区受累的危险度可能不一致,有待

与扩大患者数后再进一步验证。

总之,通过回顾性分析656例鼻咽癌患者的临床和影像学资料,我们阐明了鼻咽癌颈部淋巴结转移的规律,并发现颈部淋巴结受累侧数、淋巴结最大径、淋巴结坏死是影响远处转移和无病生存的重要因素。颈部淋巴结包膜外侵犯和颈部淋巴结受累分区,对鼻咽癌预后的价值有待进一步研究。

[参 考 文 献]

- [1] HO F C, THAM I W, EARNEST A, et al. Patterns of regional lymph node metastasis of nasopharyngeal carcinoma: a meta-analysis of clinical evidence [J]. BMC Cancer, 2012, 12: 98.
- [2] GREGOIRE V, LEVENDAG P, ANG K K, et al. CT-based delineation of lymph node levels and related CTVs in the node-negative neck: DAHANCA, EORTC, GORTEC, NCIC, RTOG consensus guidelines [J]. Radiother Oncol, 2003, 69(3): 227-236.
- [3] SPIESSL B, BEAHR S O H, HERMANEK P, et al. TNM atlas. Illustrated guide to the TNM/pTNM classification of malignant tumours [M]. Berlin Heidelberg New York: Springer, 1992.
- [4] GREGOIRE V, ANG K, BUDACH W, et al. Delineation of the neck node levels for head and neck tumors: a 2013 update. DAHANCA, EORTC, HKNPCSG, NCIC CTG, NCRI, RTOG, TROG consensus guidelines [J]. Radiother Oncol, 2014, 110(1): 172-181.
- [5] YUE D, XU Y F, ZHANG F, et al. Is replacement of the supraclavicular fossa with the lower level classification based on magnetic resonance imaging beneficial in nasopharyngeal carcinoma [J]. Radiother Oncol, 2014, 113(1): 108-114.
- [6] WANG X, HU C, YING H, et al. Patterns of lymph node metastasis from nasopharyngeal carcinoma based on the 2013 updated consensus guidelines for neck node levels [J]. Radiother Oncol, 2015, [Epub ahead of print].
- [7] VAN DEN BREKEL M W, STEL H V, CASTELIJNS J A, et al. Cervical lymph node metastasis: assessment of radiologic criteria [J]. Radiology, 1990, 177(2): 379-384.
- [8] KING A D, TSE G M, YUEN E H, et al. Comparison of CT and MR imaging for the detection of extranodal neoplastic spread in metastatic neck nodes [J]. Eur J Radiol, 2004, 52(3): 264-270.
- [9] OU X, SHEN C, KONG L, et al. Treatment outcome of nasopharyngeal carcinoma with retropharyngeal lymph nodes metastasis only and the feasibility of elective neck irradiation [J]. Oral Oncol, 2012, 48(10): 1045-1050.
- [10] 王孝深, 胡超苏, 吴永如, 等. 218例鼻咽癌颈淋巴结转移规律的影像学分析 [J]. 癌症, 2004, 23(9): 1056-1059.
- [11] MAO Y P, LIANG S B, LIU L Z, et al. The N staging system

- in nasopharyngeal carcinoma with radiation therapy oncology group guidelines for lymph node levels based on magnetic resonance imaging [J]. *Clin Cancer Res*, 2008, 14(22): 7497-7503.
- [12] PAN J, XU Y, QIU S, et al. A comparison between the Chinese 2008 and the 7th edition AJCC staging systems for nasopharyngeal carcinoma [J]. *Am J Clin Oncol*, 2015, 38(2): 189-196.
- [13] KING A D, TSE G M, AHUJA A T, et al. Necrosis in metastatic neck nodes: diagnostic accuracy of CT, MR imaging, and US [J]. *Radiology*, 2004, 230(3): 720-726.
- [14] FRIEDMAN M, ROBERTS N, KIRSHENBAUM G L, et al. Nodal size of metastatic squamous cell carcinoma of the neck [J]. *Laryngoscope*, 1993, 103(8): 854-856.
- [15] DON D M, ANZAI Y, LUFKIN R B, et al. Evaluation of cervical lymph node metastasis in squamous cell carcinoma of the head and neck [J]. *Laryngoscope*, 1995, 105(7 Pt 1): 669-674.
- [16] LAN M, HUANG Y, CHEN C Y, et al. Prognostic value of cervical nodal necrosis in nasopharyngeal carcinoma: analysis of 1800 patients with positive cervical nodal metastasis at MR imaging [J]. *Radiology*, 2015, Mar 10. [Epub ahead of print].
- [17] SNOW G B, ANNYAS A A, VAN SLOOTEN E A, et al. Prognostic factors of neck node metastasis [J]. *Clin Otolaryngol Allied Sci*, 1982, 7(3): 185-192.
- [18] COLLINS S L. Controversies in management of cancer of the neck [A] //Thawley SE PWR. *Comprehensive management of head and neck tumours* [M]. Philadelphia, PA: Saunders, 1987: 1386-1443.
- [19] HIRABAYASHI H, KOSHII K, UNO K, et al. Extracapsular spread of squamous cell carcinoma in neck lymph nodes: prognostic factor of laryngeal cancer [J]. *Laryngoscope*, 1991, 101(5): 502-506.
- [20] GREENBERG J S, FOWLER R, GOMEZ J, et al. Extent of extracapsular spread: a critical prognosticator in oral tongue cancer [J]. *Cancer*, 2003, 97(6): 1464-1470.
- [21] MYERS J N, GREENBERG J S, MO V, et al. Extracapsular spread. A significant predictor of treatment failure in patients with squamous cell carcinoma of the tongue [J]. *Cancer*, 2001, 92(12): 3030-3036.
- [22] National Comprehensive Cancer Network [M]. *Head and Neck Cancers, Version 2*, 2014.
- [23] NCCN Clinical Practice Guidelines in Oncology. head and neck cancers [EB/OL]. [2015-2-12]. http://www.nccn.org/professionals/physician_gls/f_guidelines.asp.
- [24] NG W T, LEE A W, KAN W K, et al. N-staging by magnetic resonance imaging for patients with nasopharyngeal carcinoma: pattern of nodal involvement by radiological levels [J]. *Radiother Oncol*, 2007, 82(1): 70-75.
- [25] SOM P M, CURTIN H D, MANCUSO A A. Imaging-based nodal classification for evaluation of neck metastatic adenopathy [J]. *Am J Roentgenol*, 2000, 174(3): 837-844.
- [26] LI W F, SUN Y, MAO Y P, et al. Proposed lymph node staging system using the International Consensus Guidelines for lymph node levels is predictive for nasopharyngeal carcinoma patients from endemic areas treated with intensity modulated radiation therapy [J]. *Int J Radiat Oncol Biol Phys*, 2013, 86(2): 249-256.

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