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甲状腺乳头状癌淋巴结转移的临床危险因素分析

章 锐 田 瑶 KUSH 沈文状 李兴睿 朱 智△

（华中科技大学同济医学院附属同济医院甲状腺乳腺外科 湖北 武汉 430030）

摘要 目的:探讨甲状腺乳头状癌发生颈部淋巴结转移的危险因素。**方法:**回顾性分析我院自 2017 年 1 月至 2017 年 5 月手术治疗甲状腺乳头状癌病人 177 例的临床资料，采用卡方检验、t 检验及 logistic 回归分析甲状腺乳头状癌发生颈部淋巴结的危险因素。**结果:**甲状腺乳头状癌淋巴结转移率为 45.8 %,术后并发症发生率为 6.2 %,淋巴结转移组较未转移组年龄更小、癌结节更大（P＜0.05），两组比较性别无统计学差异（P＞0.05),0.5 cm＜癌结节≤ 1 cm 组较癌结节≤ 0.5 cm 组更易出现淋巴结转移（P＜0.05),年龄大于 45 岁、癌结节≤ 0.5 cm 的患者,9.6 %发生淋巴结转移。Logistic 回归分析提示年龄、癌结节大小是淋巴结转移的独立危险因素(P＜0.05)。**结论:**年龄、癌结节大小是淋巴结转移的独立危险因素,年龄越小、癌结节越大的甲状腺乳头状癌患者,越容易出现颈部淋巴结转移。

关键词:甲状腺乳头状癌;癌结节大小;淋巴结转移

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Clinical Risk Factors of Lymph Node Metastasis in Papillary Thyroid Carcinoma

ZHANG Rui, TIAN Yao, KUSH, SHEN Wen-zhuang, LI Xing-rui, ZHU Zhi△

(Department of Thyroid and Breast Surgery, Tongji Hospital, Tongji Medical College, Huazhong University of Science and Technology, Wuhan, Hubei, 430030, China)

ABSTRACT Objective: To determine the risk factors of neck lymph node metastasis in papillary thyroid carcinoma(PTC). **Methods:** The clinical and pathologic data of 177 cases of patients who were first diagnosed as PTC in the Huazhong University of Science and Technology affiliated Tongji Hospital from January 2017 to May 2017 were retrospectively studied, Chi-square, t-test and logistic regression analysis were used to identify the risk factors of neck lymph node metastasis. **Results:** 45.8 % of the patients appeared lymph node metastasis and the incidence of postoperative complications was 6.2 %. Patients with lymph node metastasis were younger and had bigger tumor size than those without metastasis (P＜0.05). No statistical difference was found in the gender between the two groups (P＞0.05). Lymph node metastasis was more found in patients with 0.5 cm＜tumor size≤ 1 cm than thoe with tumor≤ 0.5 cm(P＜0.05). 9.6 % of the patients aged＞45 years and tumor size ≤ 0.5 cm appeared lymph node metastasis. Logistic regression analysis revealed age and tumor size were independently risk factors for the neck lymph node metastasis (P＜0.05). **Conclusions:** Age and tumor size were independently risk factors for the neck lymph node metastasis, the higher probability of lymph node metastasis was in the younger patients with bigger tumor size.

Key words: Papillary thyroid carcinoma; Tumor size; Lymph node metastasis

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前言

随着影像学的检查、细针抽吸活检技术的普及和环境因素的变化,甲状腺恶性肿瘤的发病率逐年上升[1-3],以微小乳头状癌的增加尤为明显。甲状腺乳头状癌较早就出现颈部淋巴结转移,中央区淋巴结为最常累及的部位[4,5],颈侧区淋巴结转移也较为常见。关于甲状腺乳头状癌颈部淋巴结转移的危险因素仍具有很多争议[6,7]。颈部淋巴结是否转移术前主要通过颈部淋巴结彩超[8,9],颈部 CT、磁共振检查评估[10,11],但是术前颈部淋巴结评估显示 cN0 患者术后病理证实颈部淋巴结转移并不少见[12,13]。因此,本研究主要探讨了甲状腺乳头状癌颈部淋巴结转移的危险因素、预防性中央区淋巴结清扫的必要性和甲状腺乳头状癌保守治疗的可行性。

1 材料与方法

1.1 临床资料

收集华中科技大学同济医学院附属同济医院甲状腺乳腺外科在 2017 年 1 月至 2017 年 5 月期间行双侧甲状腺全切除 + 中央区淋巴结清扫术 +/- 颈侧区淋巴结清扫术的患者，相关

作者简介:章锐(1990-),博士研究生,主要研究方向:甲状腺癌及乳腺癌,电话:13545398260,E-mail: 744170430@qq.com

△ 通讯作者:朱智,博士,主治医师,主要研究方向:甲状腺及乳腺的外科治疗,E-mail: zhzh9812014@163.com

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临床资料齐全,共计 177 例。其中男性 44 例,女性 133 例,男女比例为 1:3,T1、T2、T3、T4 分别有 160、14、3、0 例。淋巴结转移 81 例,占 45.8 %(表 1)。

1.2 手术方法

先行考虑恶性侧甲状腺腺叶及峡部切除,术中提示甲状腺乳头状癌,再行双侧甲状腺全切除术,清扫中央组淋巴结(上界:舌骨,下至胸骨上间隙,颈动脉鞘内侧至气管旁和气管前),根据术前颈部淋巴结彩超或颈部增强 CT 提示是否有颈侧区淋巴结转移,决定颈侧区淋巴结清扫。

1.3 统计学分析

所有计数资料采用卡方检验或 Fisher 确切概率法,计量资料数据以均数± 标准差表示,符合正态分布方差齐性采用 t 检验,方差不齐采用近似 t 检验,P<0.05 为差异有统计学意义。

2 结果

2.1 颈部淋巴结转移的危险因素

根据颈部淋巴结是否转移分组,淋巴结转移组年龄更小、癌结节更大、T 分期更高(表 2)。根据癌结节大小分组,0.5 cm<癌结节≤ 1 cm 组较癌结节≤ 0.5 cm 组更易出现淋巴结转移(P<0.05),癌结节≤ 0.5 cm、年龄大于 45 岁的患者发生淋巴结转移的几率为 9.6%(表 2)。

2.2 颈部淋巴结转移危险因素的 logistic 回归分析

将颈部淋巴结转移的相关危险因素纳入 logistic 回归分析,结果显示年龄、癌结节大小是淋巴结转移的独立危险因素(P<0.05)(表 3),年龄越小、癌结节越大越容易出现颈部淋巴结转移。

表 1 177 例患者的临床病理特征[例(%)]

Table 1 The clinical and pathologic data of 177 patients[n(%)]

Category	N(ratio)
Gender	
Female	133(75.1)
Male	44(24.9)
Age/year	
>45	84(47.5)
≤ 45	93(52.5)
Tumor size	
T1a	118(66.7)
T1b	42(23.7)
T2	14(7.9)
T3	3(1.7)
T4	0
Lymph node metastasis	
Yes	81(45.8)
No	96(54.2)

表 2 颈部淋巴结转移的危险因素[例(%)]

Table 2 Risk factors of neck Lymph node metastasis[n(%)]

Category	Lymph node metastasis	Non-metastasis	P
Gender			0.06
Male	26(59.1)	18(40.9)	
Female	55(41.4)	78(58.6)	
Age/year	39± 11	45± 10	0.011
>45	30(45.7)	54(64.3)	
≤ 45	51(54.8)	42(45.2)	
Tumor size	1.4± 1	0.8± 0.6	0.000
T of tumor size			0.000
T1a	39(33.1)	79(66.9)	
>0.5	25(43.9)	32(56.1)	0.016
≤ 0.5	14(23)	47(77)	
T1b	30(71.4)	12(28.6)	
≥ T2	12(70.6)	5(29.4)	

表 3 颈部淋巴结转移危险因素的 logistic 回归分析

Table 3 Logistic regression analysis for the risk factors of neck lymph node metastasis

Variables	B	SE	Walds	P	OR
Age	-0.049	0.016	9.897	0.002	0.952
Tumor size	0.869	0.243	12.825	0.000	2.385

3 讨论

甲状腺乳头状癌发病率逐年增高,多早期发生区域淋巴结转移,高达 50 %～80 %[14],本组淋巴结转移率为 45.8 %。中央区淋巴结多为颈部淋巴结转移的第一站,对为同侧颈部中央区气管前和气管旁淋巴结转移,喉返神经后方淋巴结转移较为少见[15,16]。目前国内外关于甲状腺乳头状癌颈部淋巴结转移的危险因素研究较多,并没有统一,比较公认的危险因素包括性别、年龄、肿瘤大小、包膜侵犯、病灶个数等,男性、年轻、多中心、＞0.5 cm、血管侵犯、甲状腺外生长、淋巴结外侵犯更容易出现颈部淋巴结转移[17]。虽然甲状腺乳头状癌颈部淋巴结转移率高,但是对中央区淋巴结预防性清扫仍然存在一定的争议,其原因在于临床报道的中央区淋巴结转移率差异大、缺乏长期、大样本随访资料来确定清扫转移淋巴结的获益情况、预防性中央区淋巴结清扫会增加一过性甲状旁腺功能减低的发生率[18]。

有研究表明甲状腺乳头状癌癌灶大小＜1 cm、未突破甲状腺包膜等低风险患者中央区淋巴结转移率较低,预防性清扫淋中央区淋巴结会引起较多的并发症[19,20],而且中央区淋巴结清扫不影响长期生存,对预防性中央区淋巴结清扫的意义提出质疑[21-24]。但是更多的文献支持中央区淋巴结清扫,提出淋巴结清扫能减少局部复发[25]。在本次研究中,仍有 33.1 %的甲状腺微小乳头状癌患者发生了颈部淋巴结转移,而中央组淋巴结清扫术后的总并发症只有 6.2 %,并且在短期内恢复,所以中央区淋巴结清扫时注重喉返神经、喉上神经、甲状旁腺的保护,手术仍是安全可行的。

甲状腺乳头状癌的发病具有明显的性别倾向,研究表明女性甲状腺癌发病率明显增高可能与性激素水平相关,男性患者肿瘤恶性程度要高于女性,男性甲状腺乳头状癌患者颈淋巴结转移率明显高于女性[26],这与本研究结果大致相同。本组研究中,女性患者是男性患者的 3 倍,在淋巴结转移方面,男性颈部淋巴结阳性率为 59.1 %，女性的 41.4 %，虽然百分比超过了 17.7 %,但是统计学上无明显差异。分析其原因可能在于虽然本组患者中,总样本量有 177 例,但男性患者只有 44 例,样本量偏少。

Ito 等[27]提出年龄为甲状腺乳头状癌的肿瘤生长、临床预后的指标,年轻是癌增长的独立危险因素,年长的亚临床 PMC 患者是最好的观察候选人。TNM 分期中将 45 岁作为分期评估的分界线,而 EORTC、MACIS 等系统也普遍认为 40 岁以上尤其是高龄患者更易发生转移及复发,40 岁以下患者更易发生淋巴结转移。但年龄又是预后的独立危险因素,年龄大,预后较差。本研究中,显示≤ 45 岁组较＞45 岁淋巴结转移率高,且年龄是甲状腺乳头状癌发生颈部淋巴结转移的独立危险因素,随着年龄升高,其中央区及侧颈部淋巴结转移率均呈逐渐下降趋势,年龄越小,更易发生颈部淋巴结转移[28]。

针对分化型甲状腺癌的治疗，国外不少学者提出密切观察,监视一个小的、偶然发现的甲状腺癌可能是临床上合适的选择,必要时再行手术,对合并严重的并存疾病时,推迟手术是合适的[29-31]。关于甲状腺乳头状癌保守治疗的支持性研究中,一项日本学者的前瞻性研究提出无临床淋巴结转移(cN0)、无远处转移、远离喉返神经的微小甲状腺乳头状癌的患者可予以保守治疗,彩超密切观察,1235 例病人在 60 个月内,只有 191 例(15 %)接受了手术治疗,而手术的原因包括了肿瘤的增大、发生其他的病理变化、患者选择的改变,而甲状腺肿瘤本身的增大只有 58 例(4.8 %),淋巴结转移 19 例(1.5 %)。其中,大于 40 岁的患者肿瘤进展更慢。496 例超过 60 岁的患者,只有 2.2 %出现肿瘤的增大,0.4 %出现颈部淋巴结转移[32]。另外一项同样源于日本的研究,5 年的中位观察期,230 例患者只有 7 %发生肿瘤的增长,1 %发生了淋巴结转移[33]。Tuttle 等对 291 例小于 1.5 cm 的甲状腺乳头状癌观察 6-166 个月，只有 3.8 %患者发生肿瘤增大超过 3 mm，无一例发现区域淋巴结转移和远处转移[34]。目前,国内外针对甲状腺乳头状癌的治疗仍以手术治疗为主，并没有指南支持保守治疗。本组研究中，癌结节≤ 0.5 cm、年龄大于 45 岁的甲状腺乳头状癌患者发生颈部淋巴结转移的几率为 9.6 %，远低于目前所有文献统计的甲状腺乳头状癌颈部淋巴结转移率,针对不愿手术或者基础疾病较多的这类患者，保守治疗也许是最佳选择，当肿瘤出现增大超过 3 mm 或颈部淋巴结转移,立刻手术治疗。

综上所述，甲状腺乳头状癌患者年龄越小或者癌结节越大,颈部淋巴结出现转移的几率越大,更应该行预防性中央区清扫;患者年龄越大、癌结节≤ 0.5 cm 时,不必行预防性中央区淋巴结清扫,甚至保守治疗(密切观察)也许是更佳选择。本研究不足之处在于提出≤ 0.5 cm 的肿瘤密切观察无充足的依据,在后续的研究中,将进一步观察肿瘤≤ 0.5 cm 的不愿手术的病人肿瘤大小的变化和颈部淋巴结转移情况,以期为甲状腺乳头状癌的保守治疗提供更加充分的依据。

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