基于ACR TI-RADS分类对甲状腺乳头状癌淋巴结转移风险模型的预测

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摘　要：【目的】应用美国放射学会(ACR)甲状腺影像报告及数据系统(ACR TI-RADS 2017)对甲状腺乳头状癌患者转移风险进行评估，提高超声对甲状腺转移癌检出率。【方法】回顾分析经病理确诊的甲状腺乳头状癌163例，根据术后N分期分为转移与非转移2组，对照临床和病理特征，对ACR TI-RADS评分与甲状腺乳头状癌患者发生淋巴结转移的关系进行单因素和多因素分析。【结果】发生淋巴结转移患者TI-RADS评分为12.0(10.0，14.0)，高于未发生转移的患者(P = 0.003)，多因素logistic回归结果显示超声发现淋巴结及TI-RADS评分高是甲状腺癌患者发生淋巴结转移的危险因素(对于TI-RADS评分，OR = 1.15，95% CI = 1.03-1.28，P = 0.02；对于超声发生现淋巴结，OR = 3.20，95% CI = 1.41-7.27，P = 0.01)。按单病灶或多病灶进行分层分析显示对于单病灶人群，超声发现淋巴结和TI-RADS评分高会增加甲状腺癌发生淋巴结转移的风险；而对于多病灶人群，未发现存在统计学联系。【结论】ACR TI-RADS评分结合病灶位置及数量、超声检出淋巴结等因素有利于提高甲状腺癌淋巴结转移的检出率，为临床进一步治疗提供决策。

关键词：甲状腺乳头状癌；淋巴结转移；超声；ACR TI-RADS
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Risks of Lymph Node Metastasis on Papillary Thyroid Cancer Based on ACR TI-RADS

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Abstract: 【Objective】To evaluate the risk of lymph node metastasis of papillary thyroid cancer (PTC) under the guideline of thyroid imaging report and data system (TI-RADS) published by American College of Radiology (ACR), aiming at improving the detection rate of thyroid metastatic carcinoma by combining correlative factors and ACR score 【Methods】A total of 163 patients diagnosed as papillary thyroid cancer by surgery and pathological indication were included in the study. The recruitment took place in a hospital in Shenzhen and all selected participants were divided into lymph node metastasis group and lymph node negative group respectively. Then, the information about clinical and pathological manifestation of the patients were collected before carrying multiple unconditional logistic regression test to obtain odds ratios (OR) and 95% confidence intervals (CI) between ACR TI-RADS and the risk of lymph node metastasis of PTC. 【Results】The score of TI-RADS was 12.0 (10.0, 14.0) among the patients with lymph node metastasis, higher than those without metastasis (P < 0.003). Multiple factor logistic regression illustrated that both ultrasonography detected lymph node and TI-RADS score were risk factors for lymph node metastasis in patients with thyroid carcinoma (for TI-RADS scores, OR = 1.15, 95%CI = 1.03-1.28, P = 0.02; for lymph nodes with ultrasound, OR = 3.20, 95%CI = 1.41-7.27, P = 0.01). For single lesion populations, an increased occurrence of lymph node metastasis carcinoma had been

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proved by stratified analysis when lymph node metastasis detected by ultrasonography, together with high score of TI-RADS. However there was no significance in the statistical correlation in terms of multiple lesions.【Conclusion】ACR score combined with related factors can improve thyroid metastatic carcinoma detection rate and provide therapeutic strategy for further treatment.

Key words: papillary thyroid cancer; lymph node metastasis; ultrasound; ACR TI-RADS

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甲状腺癌是最常见的内分泌恶性肿瘤,占临床发现甲状腺结节的1.6%~12.0%[1],全球范围甲状腺癌发病率呈上升趋势[2],超声是首选检查方式,其准确率达74%~82%[3-4],随着2017年美国放射学会(American College of Radiology, ACR)的发布的甲状腺影像报告及数据系统(thyroid imaging report and data system, TI-RADS)[5-7],ACR TI-RADS分类的应用有助于规范国内纷杂的TI-RADS诊断,但利用此标准预测甲状腺癌转移缺乏经验。本研究通过收集深圳市龙岗中心医院甲状腺乳头状癌(papillary thyroid cancer, PTC)病例,研究ACR TI-RADS与甲状腺乳头状癌发生淋巴结转移风险的关系,以提高甲状腺癌淋巴结转移的检出率,为临床诊断提供科学依据。

1 材料与方法

1.1 研究对象

收集2017年1月至2018年3月首次在我院进行手术并病理确诊为PTC的患者163例,平均年龄为39.8(S=10.7)岁,其中男性34例(20.9%)、女性129例(79.1%)。所有患者均签署知情同意书。本研究经本院论理委员会批准实施。按照发生颈部区域淋巴结转移分为发生淋巴结转移组和非淋巴结转移组。

1.2 研究方法

1.2.1 资料收集 通过查询病历资料,收集患者的年龄、性别、超声诊断、病灶位置、病灶数、伴随疾病、淋巴结转移等因素。

1.2.2 ACR TI-RADS得分 ACR TI-RADS由成分/结构、回声、形状/方位、边缘和局灶性强回声5个维度组成。每个维度根据病灶特征可以分别赋予0-3分,总分为0-17分。总分越高说明恶性程度越高,发生转移的风险越高(表1)。

1.2.3 超声仪器 Philips iU22、HD7; Toshiba Aplio 300; GE E8、E9超声诊断仪,探头频率7~12 MHz。

1.3 统计学方法

数据分析采用SPSS 22.0软件,所有结果以$P<0.05$为具有统计学意义。对于计量资料(年龄、TI-RADS评分)采用均数和标准差或者中位数和四分位间距进行描述,组间差异通过t检验或秩和检验分析;计数资料(性别、病灶位置等)采用例数和百分比进行描述并通过卡方分析检验组间差异。以是否发生转移为因变量,TI-RADS评分为自变量以enter法构建多因素logistic回归模型,并以Forward:LR法纳入上述单因素分析中其他有统计学意义的因素,获取变量的OR值(Odds Ratio)和95%CI(Confidence Interval)。按单病灶或多病灶进行分层,重复上述logistic回归,并获取变量的OR值和95%CI。

2 结 果

本研究甲状腺乳头状癌患者淋巴结转移率为51.3%(84/163),ACR TI-RADS评分均值(10.9±3.3)分。甲状腺乳头状癌研究人群一般特征与临床病理特征如表2-3。

发生淋巴结转移病人的TI-RADS评分高于未发生转移的病人($P=0.003$,表2)。超声发现淋巴结的病人发生转移的比例较高($P<0.001$,表2)。另外,病灶位置和病灶数在淋巴结转移和未转移的病人中分布不一致,其中双侧病灶的病人发生淋巴结转移的比例为25.0%,高于单侧病人($P=0.025$,表2),病人发生转移的风险高于单病灶病人($P=0.031$,表2)。性别、年龄、是否结节性甲状腺肿、是否桥本和是否其他伴随病与是否转移的关系无统计学意义(P值皆大于0.05,表2)。

表 1　ACR TI-RADS 得分规则

Table 1　The scoring rules of ACR TI-RADS

Score (points)	Composition (choose 1)	Echogenicity (choose 1)	Shape (choose 1)[3)]	Margin (choose 1)	Echogenic foci (choose all that apply)
0	Cystic or almost completely cystic or spongiform	Anechoic	Wider-than-tall	Smooth or Ⅲ-defined[4)]	None or large comet-tail artifacts[5)]
1	Mixed cystic and solid	Hyperechoic or isoechoic[2)]	/	/	Macrocalcification
2	Solid or almost completely solid[1)]	Hypoechoic	/	Lobulate or irregular	Peripheral (rim) calcification
3	/	Very hypoechoic	Taller-than-wide	Extra-thyroidal extension	Punctuate echogenic foci

1) Assign 2 points if composition cannot be determined because of calcification; 2) Assign 1 point if echogenicity cannot be determined; 3) This can usually be assessed by visual inspection; 4) Assign 0 point if margin cannot be determined; 5) Punctuate echogenic foci: May have small comet-tail artifacts.

表 2　甲状腺乳头状癌研究人群一般特征与临床特征

Table 2　Selected general and clinicopathological characteristics of PTC patients　n(%)

Variables	LNM(n = 84)	LNN(n = 79)	Statistic($\chi^2/t/Z$)	P
Sex			2.984	0.084
Man	22(26.2)	12(15.2)		
Women	62(73.8)	67(84.8)		
Location of lesion			5.02	0.025
One side	63(75.0)	70(88.6)		
Two sides	21(25.0)	9(11.4)		
Number of lesion			6.948	0.031
1	55(65.5)	65(82.3)		
2	18(21.4)	11(13.9)		
⩾3	11(13.1)	3(3.8)		
Nodular goiter			1.135	0.287
Yes	43(51.2)	47(59.5)		
No	41(48.8)	32(40.5)		
Thyroiditis			0.04	0.841
Yes	17(20.2)	15(19.0)		
No	67(79.8)	64(81.0)		
Other thyroid diseases[1)]			0.404	0.525
Yes	10(11.9)	7(8.9)		
No	74(88.1)	72(91.1)		
Detected LN with ultrasonic testing			11.827	< 0.001
Yes	33(39.3)	12(15.2)		
No	51(60.7)	67(84.8)		
Age/years($\bar{x} \pm s$)	38.6 ± 10.9	41.0 ± 10.4	−1.482	0.14
TI-RADS score[M(range)]	12.0(10.0,14.0)	11.0(8.0,13.0)	−2.996	0.003

LN: lymph node; LNM: Lymph node metastasis; LNN: Lymph node negative. 1) Other thyroid diseases included thyroid adenoma, parathyroid nodular hyperplasia, follicular adenoma and so on.

表3 PTC研究人群一般和病理特征与发生淋巴结转移风险的关系

Table 3 Correlation between selected general and clinicopathological characteristics and the risk of lymph node metastasis in PTC patients[1)]

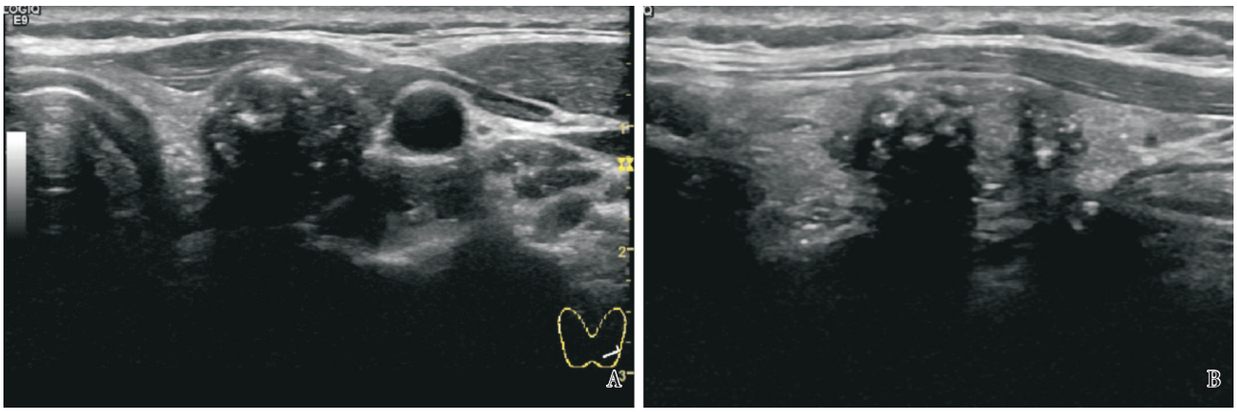
Study population	Variables	B	S.E.	Wald	*P*	OR	95%CI
Total cases							
	Age	−0.01	0.02	0.76	0.38	0.99	(0.95, 1.02)
	Sex	−0.66	0.43	2.30	0.13	0.52	(0.22, 1.21)
	TI-RADS score	0.14	0.06	5.86	0.02	1.15	(1.03, 1.28)
	Detected LN with ultrasonic testing	1.16	0.42	7.70	0.01	3.20	(1.41, 7.27)
	Location of lesion	0.15	0.77	0.04	0.85	1.16	(0.25, 5.27)
	Number of lesion[2)]			1.21	0.54		
	2	0.59	0.63	0.87	0.35	1.80	(0.52, 6.23)
	≥3	0.95	0.96	0.99	0.32	2.60	(0.40, 17.1)
Cases with single lesion[3)]							
	Age	−0.01	0.02	0.61	0.43	0.99	(0.95, 1.02)
	Sex	−0.33	0.48	0.47	0.49	0.72	(0.28, 1.85)
	TI-RADS score	0.16	0.06	5.92	0.01	1.17	(1.03, 1.32)
	Detected LN with ultrasonic testing	1.53	0.52	8.60	0.00	4.62	(1.66, 12.84)
Cases with multiple lesion							
	Age	−0.03	0.04	0.50	0.48	0.97	(0.90, 1.05)
	Sex	−20.75	14833.38	0.00	1.00	−	−
	TI-RADS score	0.11	0.13	0.79	0.37	1.12	(0.87, 1.44)
	Detected LN with ultrasonic testing	0.49	0.76	0.42	0.52	1.64	(0.37, 7.30)
	Location of lesion	0.49	0.82	0.36	0.55	1.64	(0.33, 8.19)

1) Logistic regression analysis; 2) We evaluate the association of number of lesion and the risk of lymph node metastasis with the single lesion group as the reference group; 3) The location of lesion was not included in this stratified analysis.

表3可见,总人群的分析结果显示TI-RADS评分和超声发现淋巴结是甲状腺乳头状癌患者发生淋巴结转移的危险因素,其中TI-RADS评分每增加一分,发生转移的风险增加0.15(OR = 1.15, 95%CI = 1.03-1.28),超声发现淋巴结的患者发生转移的风险是未在超声发现淋巴结的患者的3.2倍(95%CI = 1.41-7.27)。按照病灶数(单病灶和多病灶)进行分层分析,对于单病灶患者结果与总人群的结果相似,TI-RADS评分和超声发现淋巴结是患者发生转移的危险因素(对于TI-RADS评分,OR = 1.17, 95%CI = 1.03-1.32, ;对于超声发现淋巴结,OR = 4.62, 95%CI = 1.66-12.84)。对于多病灶患者,无论TI-RADS评分还是超声发现淋巴结,与发生转移风险的关系无统计学意义(对于TI-RADS评分,OR = 1.12, 95%CI = 0.87-1.44;对于超声发现淋巴结,OR = 1.64, 95%CI = 0.33-8.19)。

3 讨 论

本研究甲状腺乳头状癌患者淋巴结转移率为51.3%(84/163),高于孙庆贺[8]对2 073例甲状腺乳头状癌患者研究的转移率(45.15%);与姚瑶[9]对667例甲状腺癌临床病理分析得出48%中央区淋巴结转移率相似。本组淋巴结转移率与ACR TI-RADS评分均值(10.9 ± 3.3)相比偏高,高于ACR指南≥7分的TR5类结节,这结果与按照总人



A：Cross section；B：Sagittal section ultrasonography of papillary thyroid carcinoma and ACR TI-RADS features and scores of PTC：solid（2 points），hypoechoic（2 points），erect growth（3 points），extrathyroid invasion（3 points），bulky，marginal，punctate calcification（1+2+3 points），TI-RADS score of 16 points was classified as type Ⅴ nodule.

图1　甲状腺乳头状癌超声图像横断面和矢状面

Fig.1　Ultrasonography of papillary thyroid carcinoma（cross section and sagittal section）

群与单病灶数分层每增加TI-RADS 1分，转移风险增加0.15倍（OR = 1.15，95%CI = 1.03-1.28）一致，这就提示对高分结节病人，我们应该动态随诊，特别是对小于1 cm的结节，根据ACR TI-RADS指南要求定时复查观测结节大小、形态及颈部淋巴结的变化，必要时做细针穿刺（Fine needle puncture，FNA）明确结节性质[10-12]。

本研究从ACR TI-RADS评分结合PTC病理分析，癌体（图1）以实性结节占96.9%（158/163）；癌体回声以低和极低回声为主，占比69.9%；直立性生长的占比73.0%；边缘光滑/模糊及不能确定的只有19.0%。出现点状强回声的癌灶占比47.2%，以局灶性强回声统计≥3分的结节占70.6%，这与刘烺飚[13]的研究结果PTC钙化发生率66.7%，其中微钙化发生率为51.9%，良性病变与恶性病变之间的钙化发生率、微钙化发生率比较，差异均有统计学意义（$P < 0.01$）相符。PTC ACR TI-RADS评分统计显示，癌灶＜4分，TR4以下分类出现癌肿的几率约5.5%；ACR TI-RADS ≥ 7分TI-RADS 5类占比86.5%，发生淋巴结转移病人的TI-RADS评分高于未发生转移的病人（$P = 0.003$）。超声检查时对≥7分的结节应该重点观察，避免细节遗漏，特别是越高分值结节需做FNA，以明确结节性质，排除甲状腺癌，为避免对高分结节的假阴性出现，对非癌患者定期追访。

甲状腺乳头状癌单发病灶占73.6%（120/163），病灶数≥2个的占26.4%（43/163），与近年来的研究报道相似[14-16]；本研究以人体正中线将甲状腺分为左右两侧，单侧癌灶占81.6%（133/163），双侧癌灶占18.4%（30/163），提示在超声检查及手术中发现高度可疑（ACR TI-RADS ≥ 7分TI-RADS 5类）及FNA检出为甲状腺癌患者应该积极寻找可能存在的其他癌灶，特别是手术计划做次全切方案的病例，对计划保留的甲状腺要全面评估是否存在癌灶的可能。

多发病灶是甲状腺乳头状癌的临床特征之一，文献报道发生率为18%~87%[17-18]。本研究显示双侧病灶及病灶数≥2的病人发生转移的比例高于单病灶人群，与冯红芳的研究结果相似[19]。冯红芳[19]对1 585例甲状腺癌的临床病理特点及总结分析得出多病灶PTC患者颈部淋巴结阳性检出率为77.94%，多病灶PTC更易并发颈部淋巴结转移相符；超声检出淋巴结及TI-RADS高分结节淋巴结转移风险增加，这符合ACR指南分值越高分类越高，得癌的风险也就越高[2]。这就要求在检查过程中对甲状腺多发结节进行更加细致的独立评分，提高双侧高分结节及可疑淋巴结的检出率；本组超声检出淋巴结45例[27.6%（45/163）]，研究显示其发生转移的风险是未检出淋巴结的患者的3.20倍（95%CI = 1.41-7.27），这与文献报道的17.3%-39.4%类似[18-19]；与病理发现淋巴结51.5%存在偏差，同时两者之间的阳性符

合率只有17.8%,这提示超声检出淋巴结的难度大,在反应性增生和正常淋巴结与转移淋巴结甄别中常规超声诊断的局限性,需要借助超声造影、增强CT或其他辅助诊断,提高淋巴结检出率,特别对高分结节对转移淋巴结的预判有重要意义。

甲状腺乳头状癌伴随结节性甲状腺肿或淋巴性甲状腺炎的发生概率占64.42%(105/163),这就给甲状腺癌的超声诊断增加了难度,提示超声诊断时应对甲状腺乳头状癌与结节性甲状腺肿及淋巴性甲状腺炎的征象加以区分,重点寻找甲状腺癌ACR TI-RADS分类指标。本研究显示性别、年龄、是否结节性甲状腺肿、是否淋巴性甲状腺炎和是否其他伴随病与淋巴结转移的关系无统计学意义($P > 0.05$);而且对于多病灶患者(≥2病灶,26.4%,43/163),无论TI-RADS评分还是超声检出淋巴结,与发生转移风险的关系无统计学意义。上述结论与Kwak及陈晓康学者的研究不同[20-21],可能是由于本研究中多病灶组样本量较小,未达到检验效力。我们将增大样本继续观察明确伴随疾病对甲状腺癌的影响。

甲状腺乳头状癌采用ACR TI-RADS结合病理结果回顾性分析,得出综合利用此分类分值、双侧结节检出情况及超声淋巴结检出可以预判PTC及转移风险,为临床提供更有价值的参考意见。

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（编辑　余　菁）

本刊默认缩写与全称对照

一般地，非公知公认的缩写在正文首次出现时，应先写中文全称，然后括号注明英文全称与缩写，在中/英文摘要中使用缩写时也要先有中/英文全称与缩写对照。不过，对于以下缩写，如非表示其他含义，则本刊默认其含义如下，可不必写出其中文全称与英文全称，但在表示其他含义时必须在首次出现时与中英文全称对照。

CT：computerized tomography，计算机体层摄影术
MRI：magnetic resonance imaging，磁共振成像
ECG：electrocardiogram，心电图
PCR：polymerase chain reaction，聚合酶链反应
HE：hematoxylin and eosin，苏木精和曙红（染色）
PBS：phosphate buffered saline，磷酸缓冲液
DNA：deoxyribonucleic acid，脱氧核糖核酸
RNA：ribonucleic acid，核糖核酸
ATP：adenosine triphosphate，腺苷三磷酸
HBeAb：hepatitis B e antibody，乙型肝炎e抗体
HBeAg：hepatitis B e antigen，乙型肝炎e抗原
HBsAb：hepatitis B surface antibody，乙型肝炎表面抗体
HBsAg：hepatitis B surface antigen，乙型肝炎表面抗原
TNF：tumor necrosis factor，肿瘤坏死因子
VEGF：vascular endothelial growth factor，血管内皮生长因子
IL：interleukin，白细胞介素
HBV：hepatitis B virus，乙型肝炎病毒
HIV：human immunodeficiency virus，人类免疫缺陷病毒
WHO：World Health Organization，世界卫生组织
SD大鼠：Sprague Dawley rat，Sprague Dawley大鼠
AIDS：acquired immunodeficiency syndrome，艾滋病
CNS：中枢神经系统
CSF：脑脊液
GABA：γ-氨基丁酸
NGF：神经生长因子
AD：老年痴呆症（阿尔茨海默病）
PD：帕金森病
BBB：血脑屏障
ELISA：酶联免疫吸附测定
FBS：胎牛血清