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· 专题研究 ·

## cN0期甲状腺乳头状癌右喉返神经深层淋巴结转移的影响因素及预测模型构建

董萌, 洪晨忱, 聂昕玥, 廖仕翀, 姚峰

(武汉大学人民医院 乳腺甲状腺外科, 湖北 武汉 430060)

### 摘要

**背景与目的:** 甲状腺乳头状癌(PTC)患者往往伴有中央区淋巴结转移,单/双侧甲状腺腺叶切除加中央区淋巴结清扫(GLND)是主要的治疗手段。然而因解剖结构的差异,对于颈部淋巴结在临床上呈阴性(cN0)的PTC患者是否需要行右侧喉返神经深层淋巴结(LN-prRLN)清扫,仍存在争议。目前,有关影响cN0期PTC患者LN-prRLN转移因素的研究较少,缺乏个体化的定量预测LN-prRLN转移风险的工具。因此,本研究旨在探讨影响cN0期PTC患者LN-prRLN转移的因素,并构建个体化预测模型,以提供行LN-prRLN清扫的决策依据。

**方法:** 回顾性分析2019年6月—2022年12月武汉大学人民医院乳腺甲状腺外科行甲状腺手术的410例PTC患者的临床病理资料,按7:3的比例随机分为训练组和验证组。根据LN-prRLN术后病理转移结果,将患者分为LN-prRLN阳性组和LN-prRLN阴性组。收集患者年龄、性别、体质量指数(BMI)、甲状腺超声结果、甲状腺功能、术后病理、淋巴结转移情况等资料,并通过单因素分析及多因素Logistic回归分析确定影响cN0期PTC LN-prRLN转移的独立危险因素,根据筛选出的独立危险因素构建可视化列线图预测模型。并通过绘制ROC曲线计算曲线下面积(AUC)、校准曲线及决策曲线分析(DCA)对模型性能进行验证。

**结果:** LN-prRLN阳性组与LN-prRLN阴性组比较,单因素分析发现在肿瘤大小( $P<0.001$ )、肿瘤多灶性( $P=0.021$ )、被膜/腺外侵犯( $P=0.011$ )和右颈VIA区淋巴结阳性( $P<0.001$ )差异有统计学意义;多因素Logistic回归分析结果表明,癌灶较大( $P=0.037$ )、肿瘤多灶性( $P=0.031$ )、被膜/腺外侵犯( $P=0.033$ )、右颈VIA区淋巴结阳性( $P<0.001$ ),是cN0期PTC患者LN-prRLN转移的独立危险因素。基于上述因素建立预测模型并以可视化列线图呈现。经过验证,训练组和验证组中该模型的AUC分别为0.870(95% CI=0.807~0.933)和0.857(95% CI=0.750~0.964)。训练组和验证组的校准曲线近似于理想曲线,表明该模型的预测概率与实际概率相一致。DCA也显示,在临床中应用该模型可获得收益。

**结论:** 根据本研究所确定的cN0期PTC的LN-prRLN转移独立危险因素建立的可视化列线图预测模型有助于客观、个体化地评估颈部淋巴结,尤其是LN-prRLN的转移情况,平衡手术解剖收益和手术并发症风险,并为是否行LN-prRLN清扫提供证据,优化诊疗。

### 关键词

甲状腺癌, 乳头状; 颈淋巴结清扫术; 危险因素; 列线图  
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作者简介: 董萌, 武汉大学人民医院硕士研究生, 主要从事甲状腺肿瘤方面研究。

通信作者: 姚峰, Email: yaofengmh@163.com; 廖仕翀, Email: liaoscwhu@163.com

# Factors and predictive model construction for lymph nodes posterior to right recurrent laryngeal nerve metastasis in cN0-stage papillary thyroid carcinoma

DONG Meng, HONG Chenchen, NIE Xinyue, LIAO Shichong, YAO Feng

(Department of Breast and Thyroid Surgery, Renmin Hospital of Wuhan University, Wuhan 430060, China)

## Abstract

**Background and Aims:** Patients with papillary thyroid carcinoma (PTC) often present with central lymph node metastasis, and unilateral/bilateral thyroid lobectomy combined with central lymph node dissection (CLND) is the primary treatment approach. However, due to anatomical variations, there is still controversy regarding whether dissection of the lymph nodes posterior to right recurrent laryngeal nerve (LN-prRLN) should be performed in PTC patients with clinically negative neck lymph nodes (cN0). Currently, there is limited research on the factors influencing LN-prRLN metastasis in cN0-stage PTC patients, and there is a lack of personalized quantitative prediction tools for assessing the risk of LN-prRLN metastasis. Therefore, this study was conducted to explore the factors for LN-prRLN metastasis in cN0-stage PTC patients and develop an individualized prediction model to provide decision-making guidance for LN-prRLN dissection.

**Methods:** The clinicopathologic data of 410 patients with papillary thyroid cancer who underwent thyroid surgery at Department of Breast and Thyroid Surgery, Renmin Hospital of Wuhan University from June 2019 to December 2022 were retrospectively analyzed. The patients were randomly divided into a training group and a validation group in a 7:3 ratio. Based on the postoperative pathological results of LN-prRLN metastasis, the patients were categorized into LN-prRLN positive and LN-prRLN negative groups. Data including patient age, sex, BMI, thyroid ultrasound results, thyroid function, postoperative pathology, and lymph node metastasis were collected. Univariate analysis and multivariate Logistic regression analysis were performed to determine independent risk factors for LN-prRLN metastasis in cN0-stage PTC. A visualized prediction nomogram model was constructed based on the selected independent risk factors. The model's performance was validated by plotting the ROC curve to calculate the area under the curve (AUC), calibration curves and decision curve analysis.

**Results:** In comparison between the LN-prRLN positive group and the LN-prRLN negative group, univariate analysis revealed statistically significant differences in tumor size ( $P<0.001$ ), tumor multifocality ( $P=0.021$ ), capsular/extrathyroidal invasion ( $P=0.011$ ), and positive lymph nodes in the right neck level VIA ( $P<0.001$ ). The results of multivariate Logistic regression analysis showed that larger tumor size ( $P=0.037$ ), tumor multifocality ( $P=0.031$ ), capsular/extrathyroidal invasion ( $P=0.033$ ), and positive lymph nodes of level VIA on the right side ( $P<0.001$ ) were independent risk factors for LN-prRLN metastasis in cN0-stage PTC patients. A prediction model based on these factors was established and presented a visual nomogram. After validation, the AUC of this model in the training group and validation group were 0.870 (95% CI=0.807–0.933) and 0.857 (95% CI=0.750–0.964), respectively. The calibration curves for both the training and validation groups closely approximated the ideal curve, indicating that the predicted probabilities from the model were consistent with the actual probabilities. Decision curve analysis also demonstrated that applying this model in clinical practice resulted in clinical gains.

**Conclusion:** The visualized predictive nomogram model established based on independent risk factors

for LN-prRLN metastasis in cN0-stage PTC, as determined by this study, helps to objectively and individually assess cervical lymph nodes, particularly the metastasis of LN-prRLN. It balances the surgical anatomical benefits and the risk of surgical complications, and provides evidence for whether LN-prRLN dissection should be performed, optimizing diagnosis and treatment.

#### Key words

Thyroid Cancer, Papillary; Neck Dissection; Risk Factors; Nomograms

CLC number: R736.1

甲状腺癌是最常见的内分泌恶性肿瘤, 预计2022年我国新增甲状腺癌病例将达到224 023例。甲状腺乳头状癌(papillary thyroid carcinoma, PTC)是甲状腺癌最常见的病理类型<sup>[1]</sup>, 容易发生早期淋巴结转移(lymph node metastasis, LNM)<sup>[2]</sup>。研究<sup>[3-4]</sup>指出, 30%~90%的PTC患者伴有LNM, 而LNM与肿瘤较高的转移率及复发率有关, 可能会降低患者的术后生存率。中央区淋巴结(central compartment lymph node, CCLN)是PTC转移的第一站也是最常见的转移部位<sup>[5-6]</sup>。适当范围的颈部淋巴结清扫可有效减少PTC的局部复发, 改善预后<sup>[7-8]</sup>。对于淋巴结阳性PTC患者需要常规施行中央区淋巴结清扫(central lymph node dissection, CLND), 目前已成为国内外共识。而对于临床淋巴结阴性(clinical lymph node negative, cN0)的PTC患者是否行预防性CLND仍存在争议。为了解决这一争议, 需要对患者进行危险因素评估以确定最佳治疗方案。

考虑到PTC的高LNM率, 对于cN0期的PTC患者, 进行预防性CLND能够提供准确的术后分期, 为后续治疗指明方向, 并且可以减少颈部淋巴结复发再手术的风险。因此在我国实施预防性CLND是较为常用的手术方式<sup>[9-10]</sup>。

美国甲状腺协会及我国分化型甲状腺癌诊疗指南<sup>[10-11]</sup>概述了甲状腺癌CLND的解剖边界为喉前淋巴结、气管前淋巴结和左、右气管旁淋巴结。因解剖结构的差异, 左气管旁淋巴结位于左喉返神经(recurrent laryngeal nerve, RLN)浅层, 而右RLN将右气管旁淋巴结分为右RLN浅层淋巴结和右RLN深层淋巴结(lymph nodes posterior to right recurrent laryngeal nerve, LN-prRLN)。现有研究证据仅定义了CLND的宽度, 而没有定义其深度, 是否应该解剖LN-prRLN后的淋巴结仍存在争议。有些研究认为, LN-prRLN手术中转移率低, 手术入路复杂, 而且彻底清扫可能导致并发症发生率增高,

因此不主张常规进行LN-prRLN清扫。另有研究<sup>[7]</sup>指出, 若清扫不彻底很容易导致肿瘤的复发和转移。在首次手术中若未完全切除LN-prRLN, 则残留的淋巴结数量将显著增加, 并导致再次手术的难度以及手术并发症风险增加<sup>[12-13]</sup>。因此, 是否解剖LN-prRLN应充分平衡治疗获益和疾病风险。根据患者和肿瘤特征对LN-prRLN解剖进行个性化的手术决策可能是避免过度或治疗不足的最佳方法。现有研究<sup>[13-15]</sup>发现性别、年龄、肿瘤较大、肿瘤外侵犯及右侧RLN浅层LNM阳性等是cN0期PTC患者LN-prRLN转移的危险因素, 但难以个体化预测并量化LN-prRLN转移的概率。临床风险预测模型是一种预测某疾病结局事件发生概率的评估工具, 列线图作为可视化的多因素预测模型, 已用于多种癌症的诊断及预后, 其定量分析可以给甲状腺癌患者提供最优化的临床决策证据<sup>[16-18]</sup>。本研究回顾性分析cN0期PTC患者的临床资料, 探讨LN-prRLN转移的临床危险因素, 构建预测模型, 明确LN-prRLN转移高危患者以选择个体化的最佳手术范围。

## 1 资料与方法

### 1.1 研究对象

2019年6月—2022年12月在武汉大学人民医院乳腺甲状腺外科行甲状腺手术的患者被筛查以确定是否可以纳入研究。纳入标准:(1)病理确诊为PTC;(2)接受右侧CLND(包括LN-prRLN清扫)的右/双侧甲状腺腺叶切除术的患者;(3)术前cN0期。排除标准:(1)既往甲状腺手术、颈部手术史;(2)临床资料不完整者。最终有410例患者纳入本研究, 随机序列法将患者按7:3比例随机分为训练组和验证组。根据LN-prRLN术后病理转移结果, 将患者分为LN-prRLN阳性组和LN-prRLN阴性组。武汉大学人民医院伦理委员会规定, 对匿

名临床数据的回顾性研究不需要机构研究伦理委员会的批准,所有患者均签署了知情同意书。

## 1.2 资料收集

收集的临床数据包括:年龄、性别、体质量指数(BMI)、甲状腺功能、甲状腺超声资料、癌灶位置(右侧、左侧、双侧)、癌灶直径大小、是否有包膜/腺外侵犯、病变数目(单灶、多灶)、LNM(阳性、阴性)等临床病理资料。

## 1.3 手术操作步骤

患者在全身麻醉成功后,取仰卧位,暴露颈部,沿颈前胸骨切迹上2 cm入路取5~6 cm弧形横切口,逐层切开皮肤、皮下组织,分离颈阔肌和颈白线,切开深筋膜,暴露甲状腺。行右/双侧甲状腺切除,根据术中病理冷冻结果显示右侧或双侧PTC后,行右/双侧CLND,将右侧CCLN以右RLN为界分为右颈VIA区(浅层,即喉前、气管前淋巴结和右侧RLN浅层淋巴结)与右颈VIB区(深层,即LN-prRLN),分组送术后病理学检查。保留甲状旁腺和RLN,放置引流管并逐层缝合切口。

## 1.4 模型的建立和验证

根据上述单因素及多因素分析筛选出的cN0期PTC患者LN-prRLN转移的危险因素如癌灶较大、多灶性、被膜/腺外侵犯、右颈VIA区淋巴结阳性等,应用R语言软件(版本号:4.2.0)构建Logistic回归预测模型并绘制可视化列线图。用验证组患者数据对已构建的预测cN0期PTC患者LN-prRLN转移的列线图模型进行验证。通过绘制受试者工作特征(receiver operating characteristics, ROC)曲线,利用ROC曲线下面积(area under curve, AUC)来评价该列线图模型的预测区分能力。采用Boot-strap自举法进行1 000次重复抽样进行模型内部验证,并绘制校准曲线,评估模型预测cN0期PTC患者LN-prRLN转移的校准度。绘制决策曲线分析(decision curve analysis, DCA)评估该列线图模型用于临床是否产生净收益。

## 1.5 统计学处理

应用SPSS 25.0进行数据统计分析。正态分布者用均数±标准差( $\bar{x} \pm s$ )表示,采用 $t$ 检验,计数资料用频数(百分比)[ $n(\%)$ ]表示,采用 $\chi^2$ 检验。应用单因素分析及多因素Logistic回归筛选LN-prRLN转移的危险因素。 $P < 0.05$ 为差异有统计学意义。

## 2 结果

### 2.1 入组患者临床病理资料

本研究共纳入410例患者,其中男性90例;女性320例,平均年龄46.6岁,其中<45岁者168例,≥45岁者242例。根据术后病理结果,410例患者中右颈VIA区LNM率34.6%(142/410),LN-prRLN转移率16.3%(67/410),14.4%(59/410)的患者同时存在右颈VIA区LNM及LN-prRLN转移。右颈VIA区无转移而LN-prRLN有转移(跳跃性转移)仅占2.0%(8/410)。训练组287例PTC中,LN-prRLN阳性者45例,LN-prRLN阴性者242例;验证组123例PTC中,LN-prRLN阳性者22例,LN-prRLN阴性者101例。训练组及验证组临床资料见表1。

表1 训练组和验证组临床病理资料比较

Table 1 Comparison of clinical data between training group and validation group

资料	训练组 (n=287)	验证组 (n=123)	P
性别[n(%)]			
男	61(21.3)	29(23.6)	0.603
女	226(78.7)	94(76.4)	
年龄[岁,n(%)]			
<45	120(41.8)	48(39.0)	0.599
≥45	167(58.2)	75(61.0)	
BMI(kg/m <sup>2</sup> , $\bar{x} \pm s$ )	23.53±3.02	23.55±3.62	0.973
肿瘤大小(cm, $\bar{x} \pm s$ )	1.11±0.78	0.96±0.60	0.053
肿瘤位置[n(%)]			
右侧	163(56.8)	72(58.5)	0.744
双侧	124(43.2)	51(41.5)	
病灶数目[n(%)]			
单灶	160(55.7)	68(55.3)	0.931
多灶	127(44.3)	55(44.7)	
被膜/腺外侵犯[n(%)]			
是	123(42.9)	41(33.3)	0.071
否	164(57.1)	82(66.7)	
桥本甲状腺炎[n(%)]			
是	63(22.0)	38(30.9)	0.054
否	224(78.0)	85(69.1)	
右颈VIA区淋巴结[n(%)]			
阳性	98(34.1)	44(35.8)	0.751
阴性	189(65.9)	79(64.2)	
LN-prRLN[n(%)]			
阳性	45(15.7)	22(17.9)	0.580
阴性	242(84.3)	101(82.1)	

## 2.2 训练组LN-prRLN转移的危险因素分析

单因素分析发现,训练组中LN-prRLN阳性组与阴性组在肿瘤大小 ( $P<0.001$ )、多灶性 ( $P=0.021$ )、被膜/腺外侵犯 ( $P=0.011$ ) 和右颈VIA区淋巴结阳性 ( $P<0.001$ ) 差异有统计学意义(表2)。将上述单因素分析筛选出的具有统计学意义的指标进行多因素 Logistic 回归分析。结果表明癌灶较大 ( $P=0.037$ )、多灶性 ( $P=0.031$ )、被膜/腺外侵犯 ( $P=0.033$ )、右颈VIA区淋巴结阳性 ( $P<0.001$ ) 是cN0期PTC患者LN-prRLN转移的独立危险因素(表3)。

表2 训练组LN-prRLN转移的单因素分析

Table 2 Univariate analysis of factors for LN-prRLN metastasis in training group

资料	阳性(n=45)	阴性(n=242)	P
性别[n(%)]			
男	12(26.7)	49(20.2)	0.334
女	33(73.3)	193(79.8)	
年龄[岁, n(%)]			
<45	24(53.3)	96(39.7)	0.088
≥45	21(46.7)	146(60.3)	
BMI(kg/m <sup>2</sup> , $\bar{x} \pm s$ )	24.08±3.24	23.43±2.98	0.191
肿瘤大小(cm, $\bar{x} \pm s$ )	1.56±1.02	1.03±0.70	<0.001
肿瘤位置[n(%)]			
右侧	30(66.7)	133(45.0)	0.145
双侧	15(33.3)	109(55.0)	
病灶数目[n(%)]			
单灶	18(40.0)	142(58.7)	0.021
多灶	27(60.0)	100(41.3)	
被膜/腺外侵犯[n(%)]			
是	27(60.0)	96(39.7)	0.011
否	18(40.0)	146(60.3)	
桥本甲状腺炎[n(%)]			
是	14(31.1)	49(20.2)	0.106
否	31(68.9)	193(79.8)	
右颈VIA区淋巴结[n(%)]			
阳性	39(86.7)	59(24.4)	<0.001
阴性	6(13.3)	183(75.6)	

表3 训练组LN-prRLN转移的多因素回归分析

Table 3 Multivariate regression analysis of factors for LN-prRLN metastasis in training group

因素	$\beta$	P	OR(95 CI)
肿瘤大小	0.454	0.037	1.575(1.028~2.413)
多灶性	0.867	0.031	2.379(1.084~5.220)
被膜/腺外侵犯	0.860	0.033	2.364(1.071~5.219)
右颈VIA区淋巴结阳性	3.105	<0.001	22.316(8.586~58.004)

## 2.3 cN0期PTC LN-prRLN转移预测模型的构建及验证

2.3.1 预测模型构建 基于上述多因素二元 Logistic 回归筛选出的独立影响因素(表3),应用R语言构建可视化的cN0期PTC合并LN-prRLN转移的预测列线图模型。每个影响因素比对应分值标尺单独得出分数后计算总得分,比对列线图下方总分标尺可得到相应的LN-prRLN转移的预测概率(图1)。

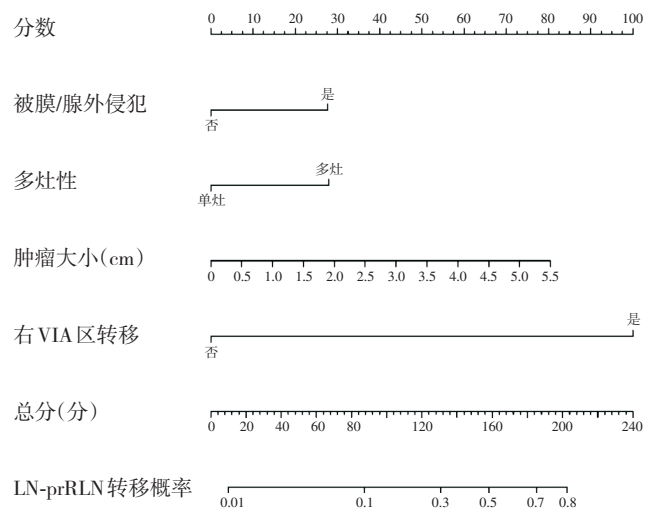


图1 预测cN0期PTC LN-prRLN转移的列线图模型

Figure 1 Nomogram model for LN-prRLN metastasis in cN0 stage PTC

2.3.2 预测模型的验证 列线图 ROC 曲线结果显示,训练组的AUC为0.870 (95% CI=0.807~0.933);验证组的AUC为0.857 (95% CI=0.750~0.964),说明列线图模型预测LN-prRLN转移区分能力较好,表明列线图具有良好的判别性能(图2)。采用 Boot-strap 自举法进行数据1 000次重复抽样进行模型内部验证,列线图预测的cN0期PTC患者LN-prRLN转移的概率绘制在x轴上,实际概率绘制在y轴上。45度线表示模型的理想预测曲线,实线表示预测列线图的实际预测性能,训练组和验证组校准曲线较趋近于理想曲线,表明该模型预测概率与实际概率一致性较好(图3)。训练组和验证组示列线图的DCA如下(图4)。黑色虚线表示所有患者都是LN-prRLN转移的假设;而黑色实线代表没有患者是LN-prRLN转移的假设;红色实线表示cN0期PTC患者LN-prRLN转移风险概率。决策曲线显示,列线图在训练组和验证组中都产生了净收益,使用列线图预测cN0期PTC患

者 LN-prRLN 转移比单独使用任何其他预测因子 具有良好的应用价值。增加更多的净收益，表明该模型在临床决策方面

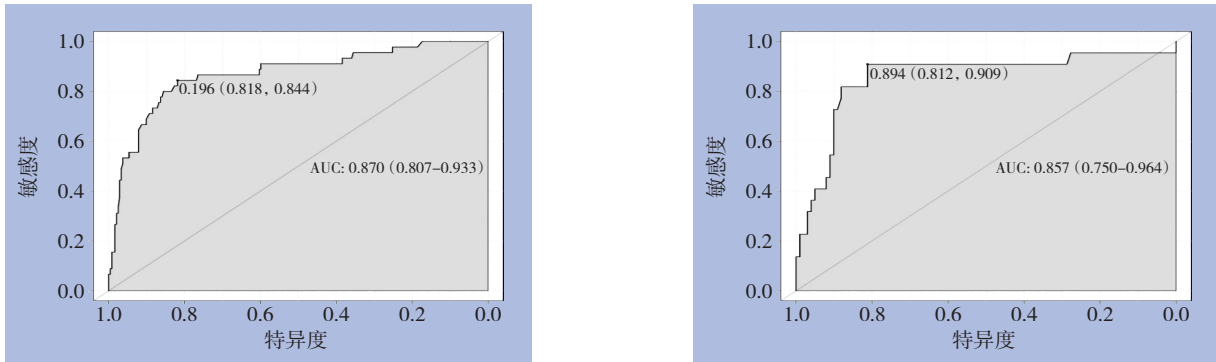


图2 训练组和验证组的ROC曲线  
Figure 2 The ROC curves of the training group and validation group

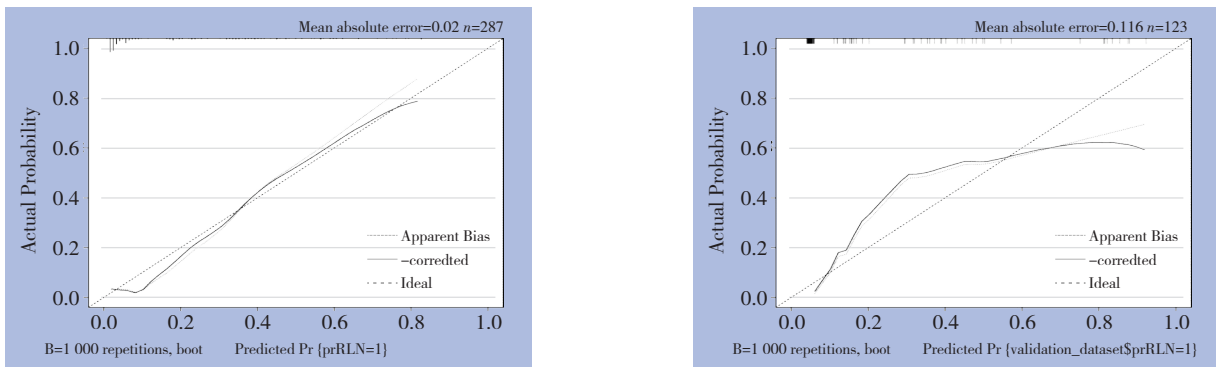


图3 训练组和验证组的校准曲线  
Figure 3 The calibration curves of the training group and validation group

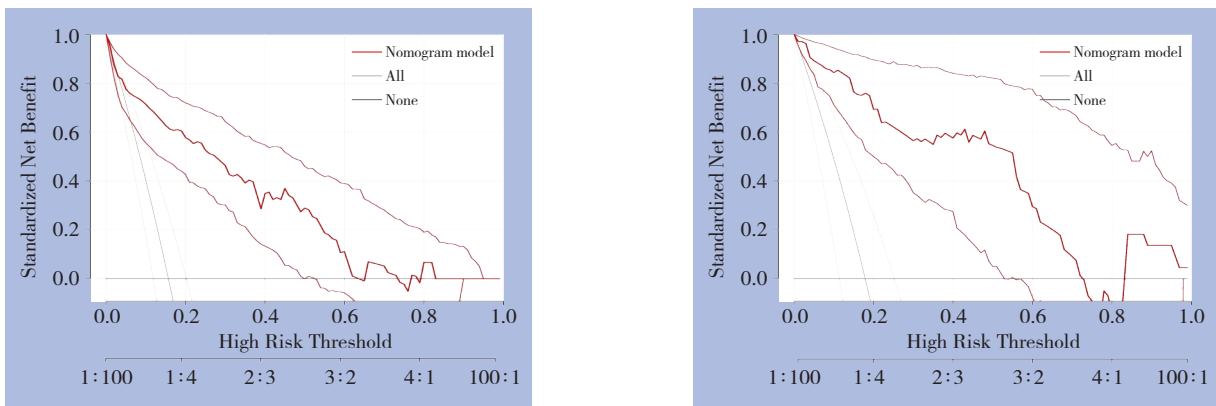


图4 训练组和验证组的DCA曲线  
Figure 4 DCA curves of the training group and validation group

### 3 讨论

PTC 预后良好但易发生 LNM，以 CCLN 转移最为常见。单/双侧甲状腺腺叶切除+CLND 是我国 PTC 的主要手术方式，但 CLND 的范围仍存在争议。ATA 将 CLND 边界定义为：外界为颈动脉，内侧界为气管边缘，上界至舌骨，下界至胸骨切迹，

包括喉前淋巴结、气管前淋巴结和左、右气管旁淋巴结<sup>[1]</sup>。因解剖结构的差异，右 RLN 比左 RLN 走行更浅，通过右中隔室的纤维脂肪组织上行，将右 CLND 分为右 RLN 浅层淋巴结（右颈 VIA 区）和 LN-prRLN（右颈 VIB 区）。因 LN-prRLN 位于右 RLN 的后方，位置较深，被脂肪组织包裹，在切除 LN-prRLN 的过程中，牵引和抬高 RLN 可能会增

加右RLN的损伤,此外右RLN后方区域的淋巴组织和邻近脂肪组织的剥离可能会导致其他并发症,如甲状旁腺损伤和乳糜瘘等。且因LN-prRLN解剖位置较深,术前超声敏感性较差,难以在术前明确是否有转移<sup>[19]</sup>。因此对于cN0期PTC患者是否常规行LN-prRLN清扫目前仍存在较大争议<sup>[13]</sup>。部分学者<sup>[20-22]</sup>认为LN-prRLN转移率低,暴露范围深且窄,彻底清扫并发症发生率高,需要更有经验的手术团队才能安全解剖,无须常规进行LN-prRLN清扫;也有学者提出,PTC患者的LN-prRLN转移率高达2.74%~38.27%,首次手术若不完全清扫,可能加速肿瘤复发,增加二次手术难度。而适当范围的CLND能降低肿瘤局部复发率和术后并发症的发生率。对于cN0期PTC患者来说,预防性CLND的范围仍然存在争议。在确定适当的颈淋巴结清扫范围时,应充分考虑减少肿瘤复发和术后并发症的发生率。因此在术前和术中的评估过程中,有必要分析cN0期PTC患者LN-prRLN转移的危险因素,对有高危因素的患者进行甄别,确定手术范围,以便外科医生做出最佳手术选择。

本研究中,右颈VIA区LNM率为34.6%,LN-prRLN的LNM发生率为16.3%,14.4%的患者同时存在右颈VIA区及VIB区LNM,右颈VIA区无转移而LN-prRLN有转移仅占比2.0%,与既往研究相符<sup>[10]</sup>。本研究回顾性分析cN0期PTC患者的临床病理信息,提供单因素分析发现LN-prRLN转移与肿瘤较大、多灶性、被膜/腺外侵犯和右颈VIA区淋巴结阳性存在统计学差异。多因素Logistic回归分析结果表明癌灶较大、多灶性、被膜/腺外侵犯、右颈VIA区淋巴结阳性是cN0期PTC LN-prRLN转移的独立危险因素,与既往研究相同。多项研究<sup>[23-24]</sup>认为PTC患者中女性发病率较高,但男性患者的肿瘤侵犯性更强,男性更易出现LN-prRLN转移。一项Meta分析<sup>[13]</sup>结果也显示性别与LN-prRLN转移相关,且这种相关性可能与样本量增加有关。Hou和Zhang等<sup>[25-26]</sup>还发现年龄<45岁的患者较年老患者更易发生LN-prRLN转移。本研究单因素及多因素回归分析显示男性和年龄<45岁均不是LN-prRLN转移的危险因素,分析其原因可能与样本量不足有关。

有研究<sup>[27-28]</sup>发现肿瘤直径与LN-prRLN转移率呈正相关,肿瘤越大,转移率越高。Zhou等<sup>[29]</sup>也发现肿瘤>1 cm会增加LN-arRLN的转移风险。Yuan

等<sup>[22]</sup>还发现所有肿瘤>2.0 cm的患者均有LN-prRLN转移,认为肿瘤>2.0 cm是PTC患者LN-prRLN转移的重要预测因子。最近的一项Meta分析<sup>[13]</sup>也指出肿瘤大小是LN-prRLN转移的独立风险因素,与本研究结果一致。故术前超声或术中发现癌灶较大的患者,在进行CLND时,应进行LN-prRLN的清扫。研究<sup>[13]</sup>指出肿瘤多灶性不仅与LN-prRLN转移有关,而且与PTC患者的预后密切相关。一项Meta分析<sup>[30]</sup>也表明,肿瘤多灶性不仅是疾病进展的重要危险因素,还会增加疾病复发的风险。既往研究<sup>[31]</sup>也发现若肿瘤侵犯或突破被膜,患者的10年生存率明显降低。此外,当癌灶侵犯被膜或甲状腺外组织时,肿瘤转移风险增大,通常会增加LN-prRLN转移的风险,应彻底清扫LN-prRLN<sup>[14]</sup>。所以术前明确癌灶是否有腺外侵犯是十分重要的,既往研究也证实超声对评估肿瘤数目及肿瘤的腺外侵犯具有极好的预测价值<sup>[23]</sup>。故术前超声发现多灶肿瘤及肿瘤侵犯或突破甲状腺被膜的患者,应常规行LN-prRLN的清扫,以降低清扫不完全复发的风险。同样,我们的研究结果也证明癌灶较大、肿瘤多灶性和被膜/腺外侵犯是LN-prRLN转移的独立危险因素,对于伴有上述危险因素的患者,在临床中应充分平衡手术获益与手术并发症的矛盾,精细手术操作,行LN-prRLN切除。

本研究发现410例患者中仅有8例为右颈VIA区无转移而LN-prRLN有转移,占比2.0%。与本研究相似,多项研究<sup>[13-14, 26-27, 29]</sup>发现PTC颈部LNM时较少出现右颈VIA区无转移而LN-prRLN有转移的情况,还发现有右颈VIA区LNM的患者发生LN-prRLN转移的风险几乎是没有任何右颈VIA区LNM的患者的两倍,都提示右颈VIA区LNM是LN-prRLN转移重要的独立危险因素。甲状腺癌术前对右颈VIA区淋巴结行影像学,可有效预测LN-prRLN的转移情况,确定手术清扫范围。对于术前超声结果不明确者,可行右颈VIA区淋巴结术中快速冷冻,进一步明确肿瘤LNM情况,对于发现有右颈VIA区LNM的患者,在进行CLND时应切除LN-prRLN<sup>[32]</sup>。在确定LN-prRLN转移的危险因素后,通过R语言建立了预测LN-prRLN转移的列线图模型,经验证明该模型效能良好。在临床中,术前超声报告、术中探查及术中快速冷冻检查,都有助于医生获取临床病理信息,预测LN-prRLN的转移情况。临床医生可根据此列线图模型,量

化LN-prRLN转移的概率, 决定手术范围。

综上所述, 本研究发现癌灶较大、肿瘤多灶性、被膜/腺外侵犯、右颈VIA区LNM是cN0期PTC LN-prRLN转移的独立危险因素。基于临床病理特征建立了预测LN-prRLN转移的预测模型, 该模型可客观、个体化地预测cN0期PTC患者LN-prRLN的转移风险, 平衡手术解剖收益和风险, 提高治疗决策。本研究的局限在于本研究是一项单中心的回顾性研究, 样本量有限, 只进行了内部验证, 缺乏外部验证, 有待下一步多中心研究验证。

利益冲突: 所有作者均声明不存在利益冲突。

作者贡献声明: 董萌负责查阅文献、起草和撰写文章; 董萌、洪晨忱和聂昕玥收集临床资料并完成数据分析和图表制作, 姚峰和廖仕翀负责本研究课题的构思和设计, 指导文稿撰写并对文稿的内容进行审阅。

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