



doi:10.7659/j.issn.1005-6947.2023.05.008
http://dx.doi.org/10.7659/j.issn.1005-6947.2023.05.008
China Journal of General Surgery, 2023, 32(5):690-697.

· 专题研究 ·

细针穿刺洗脱液甲状腺球蛋白检测对甲状腺乳头状癌颈部淋巴结转移的诊断价值

王亚楠¹, 张欢^{1,2}, 欧阳向柳³, 韩云霞³, 刘丽云⁴, 郑立春¹

(河北省唐山市工人医院 1. 核医学科 3. 超声医学科 4. 病理科, 河北 唐山 063000; 2. 华北理工大学 研究生学院, 河北 唐山 063210)

摘要

背景与目的: 目前判断甲状腺乳头状癌 (PTC) 颈部淋巴结转移主要依靠超声及细针穿刺抽吸活细胞学检查 (FNAC), 但均存在主观性及局限性。本研究探讨超声引导下细针穿刺抽吸活检洗脱液中甲状腺球蛋白 (FNA-Tg) 检测在 PTC 患者颈部淋巴结转移中的应用价值。

方法: 回顾性分析术后病理确诊的 144 例 PTC 患者资料, 术前均行血清甲状腺球蛋白 (Tg) 检测, 可疑颈部淋巴结行超声引导下 FNAC 及 FNA-Tg 检测, 以术后最终病理结果为金标准, 比较 FNAC、FNA-Tg 及两者联合对 PTC 患者颈部淋巴结转移诊断的敏感度、特异度、准确性、阳性预测值及阴性预测值, 并绘制各诊断方法的受试者特征 (ROC) 曲线, 计算 ROC 曲线下面积 (AUC), 确定定量指标 FNA-Tg 最佳诊断阈值。

结果: 144 例 PTC 患者共检测 176 枚淋巴结, 最终经病理诊断 PTC 转移性淋巴结 81 枚, 非转移性淋巴结 95 枚。转移性淋巴结组血清 Tg、FNA-Tg 分别为 28.84 (7.42~84.22) ng/mL、500 (142.56~500) ng/mL, 非转移性淋巴结组血清 Tg、FNA-Tg 分别为 20.11 (9.57~38.30) ng/mL、0.10 (0.10~0.29) ng/mL, 两组间血清 Tg 比较差异无统计学意义 ($Z=1.878$, $P=0.062$), 两组间 FNA-Tg 比较差异有统计学意义 ($Z=10.981$, $P<0.001$)。FNA-Tg 诊断 PTC 转移性淋巴结的 ROC 曲线 AUC 为 0.964 (95% CI=0.937~0.992, $P<0.001$), 最佳诊断阈值为 4.79 ng/mL, FNAC 诊断 PTC 转移性淋巴结的 ROC 曲线 AUC 为 0.840 (95% CI=0.777~0.903, $P<0.001$); FNA-Tg 和 FNAC 两者联合诊断 PTC 转移性淋巴结的 ROC 曲线 AUC 为 0.960 (95% CI=0.927~0.994, $P<0.001$)。FNAC 及 FNA-Tg 诊断 PTC 转移性淋巴结的诊断敏感度、特异度、准确性、阳性预测值及阴性预测值分别为 81.48%、85.26%、83.52%、82.50%、84.38% 和 92.59%、93.68%、93.18%、92.59%、93.68%; FNA-Tg 和 FNAC 两者联合应用时为 96.30%、95.79%、96.02%、95.12%、96.81%。FNAC 与 FNA-Tg 在敏感度、准确性及阴性预测值差异有统计学意义 ($\chi^2=4.432$, $P=0.035$; $\chi^2=7.798$, $P=0.005$; $\chi^2=4.228$, $P=0.040$), 在特异度及阳性预测值则差异无统计学意义 ($\chi^2=3.576$, $P=0.059$; $\chi^2=3.768$, $P=0.052$), FNA-Tg 和 FNAC 两者联合时各项诊断指标均有所提高。

结论: FNA-Tg 测定为客观定量诊断方式, 对诊断 PTC 颈部淋巴结转移具有较高的诊断价值, 且高于 FNAC, FNA-Tg 测定与 FNAC 联合应用时可进一步提高诊断效能。

关键词

甲状腺癌, 乳头状; 活组织检查, 细针; 甲状腺球蛋白; 淋巴转移

中图分类号: R736.1

基金项目: 河北省 2020 年度医学科学研究课题计划基金资助项目 (20201517)。

收稿日期: 2022-09-28; **修订日期:** 2023-04-28。

作者简介: 王亚楠, 河北省唐山市工人医院主管检验师, 主要从事甲状腺相关激素检验方面的研究。

通信作者: 郑立春, Email: nmzhenglch@163.com

Diagnostic value of thyroglobulin detection in washout fluid of fine-needle aspiration biopsy for cervical lymph node metastasis in papillary thyroid carcinoma

WANG Yanan¹, ZHANG Huan^{1,2}, OUYANG Xiangliu³, HAN Yunxia³, LIU Liyun⁴, ZHENG Lichun¹

(1. Department of Nuclear Medicine 3. Department of Ultrasound Medicine 4. Department of Pathology, Tangshan Gongren Hospital, Tangshan, Hebei 063000, China; 2. Graduate School, North China University of Science and Technology, Tangshan, Hebei 063210, China)

Abstract

Background and Aims: The current diagnosis of neck lymph node metastasis in papillary thyroid carcinoma (PTC) relies mainly on ultrasound and fine-needle aspiration cytology (FNAC). However, both methods have subjectivity and limitations. This study was conducted to investigate the application value of detection of thyroglobulin in the washout fluid from fine-needle aspiration biopsy (FNA-Tg) under ultrasound guidance for cervical lymph node metastasis in PTC patients.

Methods: The data of 144 patients with pathologically confirmed PTC were retrospectively analyzed. Preoperatively, all patients underwent serum thyroglobulin (Tg) testing, and suspicious cervical lymph nodes were subjected to ultrasound-guided FNAC and FNA-Tg testing. The postoperative final pathological results were considered as the gold standard. The sensitivity, specificity, accuracy, positive predictive value, and negative predictive value of FNAC, FNA-Tg, and their combination in diagnosing neck lymph node metastasis in PTC patients were compared. Receiver operating characteristic (ROC) curves were plotted for each diagnostic method, and the area under the ROC curve (AUC) was calculated to determine the optimal diagnostic threshold for the quantitative parameter FNA-Tg.

Results: A total of 176 lymph nodes were examined in 144 PTC patients. Among them, 81 lymph nodes were diagnosed as metastatic PTC and 95 lymph nodes were non-metastatic. The serum Tg and FNA-Tg levels in the metastatic lymph node group were 28.84 (7.42–84.22) ng/mL and 500 (142.56–500) ng/mL, respectively. In the non-metastatic lymph node group, the serum Tg and FNA-Tg levels were 20.11 (9.57–38.30) ng/mL and 0.10 (0.10–0.29) ng/mL, respectively. There was no statistically significant difference in serum Tg between the two groups ($Z=1.878$, $P=0.062$), while there was a statistically significant difference in FNA-Tg between the two groups ($Z=10.981$, $P<0.001$). The AUC of ROC curve for FNA-Tg in diagnosing metastatic PTC lymph nodes was 0.964 (95% $CI=0.937-0.992$, $P<0.001$), with the optimal diagnostic cut-off value of 4.79 ng/mL. The AUC of ROC curve for FNAC in diagnosing metastatic PTC lymph nodes was 0.840 (95% $CI=0.777-0.903$, $P<0.001$). When FNA-Tg and FNAC were used together to diagnose metastatic PTC lymph nodes, the AUC of ROC curve was 0.960 (95% $CI=0.927-0.994$, $P<0.001$). The diagnostic sensitivity, specificity, accuracy, positive predictive value, and negative predictive value in diagnosing metastatic PTC lymph nodes were 81.48%, 85.26%, 83.52%, 82.50%, 84.38% for FNAC, and 92.59%, 93.68%, 93.18%, 92.59%, 93.68% for FNA-Tg, respectively. When FNA-Tg and FNAC were used together, the values were 96.30%, 95.79%, 96.02%, 95.12%, and 96.81%. There were statistically significant differences in sensitivity, accuracy, and negative predictive value between FNAC and FNA-Tg ($\chi^2=4.432$, $P=0.035$; $\chi^2=7.798$, $P=0.005$; $\chi^2=4.228$, $P=0.040$). However, there was no statistically significant difference in specificity and positive predictive value ($\chi^2=3.576$, $P=0.059$; $\chi^2=3.768$, $P=0.052$). and all diagnostic indicators were improved by the combination of FNA-Tg and FNAC.

Conclusion: FNA-Tg measurement is an objective quantitative diagnostic method that has high diagnostic value in detecting cervical lymph node metastasis in PTC. It is superior to FNAC, and when FNA-Tg measurement is combined with FNAC, it further enhances the diagnostic performance.

Key words

Thyroid Cancer, Papillary; Biopsy, Fine-Needle; Thyroglobulin; Lymphatic Metastasis

CLC number: R736.1

甲状腺癌发病率约占全世界所有癌症的3.1%^[1],是最常见的内分泌恶性肿瘤,其发病率也是呈现逐年上升的趋势,我国国家癌症中心开展的中国恶性肿瘤最新流行情况分析^[2]显示,我国甲状腺癌的发病率为14.6/10万,其中大多数为分化型甲状腺癌(differentiated thyroid cancer, DTC),而常见的病理类型为甲状腺乳头状癌^[3](papillary thyroid carcinoma, PTC)。明确颈部淋巴结是否存在转移对于临床TNM分期、手术方案的选择及患者预后至关重要^[4],而PTC往往约20%~50%都存在淋巴结转移^[5-6],所以正确判断PTC颈部淋巴结转移情况显得尤为重要。目前判断淋巴结转移主要依靠超声检查及超声引导下细针穿刺抽吸活检细胞学检查(fine-needle aspiration cytology, FNAC),FNAC能有效鉴别甲状腺癌患者颈部淋巴结良恶性^[7],但仍存在局限性,诊断效能受操作者经验、取材及涂片质量等因素影响,在转移性淋巴结血供丰富或大部分实质囊性变的情况下,很难获得足够的标本,假阴性率较高^[8],失败率可到近20%,有研究表明FNAC联合基因检测能提高诊断准确性,如*BRAF*^{V600E}、*RAS*基因等,但其检测费用较高,临床普及应用较困难。近期越来越多的学者^[9-12]将细针穿刺抽吸活检洗脱液中甲状腺球蛋白(fine-needle aspiration-thyroglobulin, FNA-Tg)进行研究,测定其FNA-Tg数值来诊断PTC转移淋巴结,操作简便,其检测不受主观因素影响,具有较高的诊断能力,降低了假阴性率,避免了漏诊,已成为目前研究热点,有研究表明FNA-Tg诊断价值优于FNAC,两者联合检测时诊断价值优于单一FNAC或FNA-Tg检测,其诊断敏感度和特异度几乎接近100%。本文将进一步总结分析FNAC、FNA-Tg及两者联合应用时对PTC患者颈部淋巴结转移的诊断价值。

1 资料与方法

1.1 一般资料

选取2019年1月—2021年12月河北省唐山市工人医院手术病理确诊的PTC伴颈部可疑淋巴结转移的患者144例,共176枚淋巴结为研究对象,其中男性42例、女性102例;年龄15~75(48.68±12.96)岁。纳入标准:(1)经术后病理确诊为PTC;(2)转移性淋巴结病理为PTC;(3)术前对可疑淋巴结行超声引导下FNAC及FNA-Tg检测;(4)可疑淋巴结具有明确术后病理。排除标准:(1)病理类型非PTC患者;(2)术前颈部淋巴结未行FNAC及FNA-Tg;(3)淋巴结无术后明确病理;(4)转移性淋巴结病理为非PTC。本研究方案经由唐山市工人医院伦理委员会审批(批号:GRYY-LL-2019-38),并取得患者的知情同意。

1.2 FNAC及仪器

穿刺前1周停用抗凝药,并完善血常规及出凝血时间检测。由经验丰富的高年资医师进行穿刺操作,采用Philips EPIQ 7型超声诊断仪,频率为5~12 MHz,使用线阵探头,患者仰卧位,充分暴露预穿刺部位,常规消毒、铺巾,2%利多卡因局部麻醉;利用超声扫查颈部淋巴结的回声、大小、形态、血流情况及内部结构等信息,对可疑淋巴结在超声引导下采用20 G穿刺针穿刺病灶(抽吸淋巴结边缘实性部分),针尖进入目标病灶后反复提插、旋转抽吸(反复多点抽吸3次以上),当有血性液体吸入注射器内时立即拔针;将穿刺液进行涂片和注入试管处理,送病理科进行细胞学检查(图1)。穿刺结束后局部按压15 min。

1.3 FNA-Tg的制备及甲状腺球蛋白(Tg)检测

在超声引导下对可疑淋巴结采用20 G穿刺针穿刺病灶(抽吸淋巴结边缘实性部分),针尖进入目标病灶后反复提插、旋转抽吸(反复多点抽吸3次以上),将穿刺液进行细胞学涂片后再进行FNA-Tg的制备:将涂片后的穿刺针在提前准备好的装有

1 mL生理盐水普通无添加剂管里反复(3次以上)冲洗、抽吸穿刺针及针筒,将残留在针筒及穿刺针中的穿刺液冲洗干净,并用力振摇后送核医学科进行检测;收集同期患者静脉血5 mL,常温下离心速度为3 000 r/min离心5 min,达到血清分离后进行上机检测。采用全自动化学发光免疫分析进行洗脱液Tg及血清Tg含量检测,检测设备为Mindray CL-2000i仪器,该设备检测结果上限值为

500 ng/mL,若检测结果大于上限值时该结果记为500 ng/mL。FNA-Tg诊断标准参考美国甲状腺学会(ATA)《成人甲状腺结节与分化型甲状腺癌诊治指南》^[13],具体如下:FNA-Tg<1 ng/mL,诊断为阴性;FNA-Tg>10 ng/mL时诊断为阳性;当FNA-Tg在1~10 ng/mL时,FNA-Tg/血清Tg<1诊断为阴性,FNA-Tg/血清Tg>1诊断为阳性。

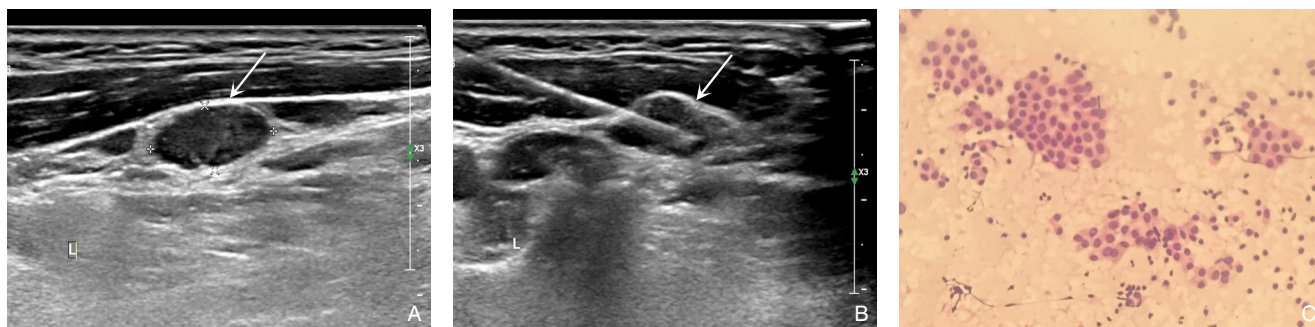


图1 典型病例资料(女,41岁,左颈部III区转移性淋巴结) A:转移淋巴结常规超声图像;B:转移淋巴结FNAC图像(箭头所示);C:细胞学病理(HE×200)

Figure 1 Typical case data (female, 41 years old, metastatic lymph node in the left level-III neck) A: Conventional ultrasound image of the metastatic lymph node; B: FNAC image of the metastatic lymph node (indicated by an arrow); C: Cytological pathology (HE×200)

1.4 穿刺淋巴结的标记

超声引导下对淋巴结穿刺后,并采用细针在穿刺淋巴结内注入约0.1~0.2 mL纳米炭混悬液(重庆莱美医药有限公司生产)进行标记,并同时详细记录该淋巴结的大小及所在位置,以便手术切除过程中能够准确找到该标记的淋巴结。

1.5 统计学处理

应用SPSS 20.0软件进行数据统计分析。计量资料符合正态分布的以均数±标准差($\bar{x} \pm s$)表示,组间比较采用 t 检验;不符合正态分布的计量资料以中位数(四分位间距)[$M(IQR)$]表示,组间比较采用Mann-Whitney U 检验;以术后病理结果为标准,绘制各种诊断方法(FNAC、FNA-Tg及两者联合)的受试者特征曲线(ROC),计算曲线下面积(AUC),并确定FNA-Tg最佳诊断阈值;计数资料以频数、率表示,计算各种诊断方法的敏感度、特异度、准确性、阳性预测值及阴性预测值,组间比较采用 χ^2 检验或 F 精确概率法检验。两者联合诊断时以其中任何一种(FNAC或FNA-Tg)结果为阳性时即诊断为阳性,两者结果均为阴性时诊断为阴性。 $P<0.05$ 为差异有统计学意义。

2 结果

2.1 病理结果

144例患者术后病理类型均为PTC,超声引导下共穿刺176枚淋巴结,淋巴结长径为0.6~1.9 cm,最终通过术后组织病理学确定转移性淋巴结81枚,病理为淋巴结转移性PTC,非转移性淋巴结95枚,病理为淋巴结淋巴组织反应性增生。淋巴结位置及数量分别为I区3枚、II区14枚、III区67枚、IV区83枚、V区6枚、VI区3枚。

2.2 血清Tg及FNA-Tg

转移组血清Tg范围为0.10~500 ng/mL,中位数为28.84(7.42~84.22) ng/mL,FNA-Tg范围为0.10~500 ng/mL,中位数为500(142.56~500) ng/mL;非转移组血清Tg范围为0.10~493.93 ng/mL,中位数为20.11(9.57~38.3) ng/mL,FNA-Tg范围为0.10~170.28 ng/mL,中位数为0.10(0.10~0.29) ng/mL。两组间血清Tg差异无统计学意义($Z=1.878, P=0.062$),FNA-Tg差异有统计学意义($Z=10.981, P<0.001$)。对三种诊断方法进行ROC曲线分析,FNA-Tg的ROC曲线AUC)为0.964(95% CI=0.937~

0.992, $P<0.001$), 最佳诊断阈值为 4.79 ng/mL; FNAC 的 ROC 曲线 AUC 为 0.840 (95% $CI=0.777\sim$ 0.903, $P<0.001$); 两者联合 ROC 曲线 AUC 为 0.960 (95% $CI=0.927\sim 0.994$, $P<0.001$) (表 1) (图 2)。

表 1 FNAC、FNA-Tg 及两者联合对 PTC 患者颈部淋巴结的诊断结果与病理结果比较 [n (%)]

Table 1 Comparison of pathological results to diagnostic results of FNAC, FNA-Tg and their combination for cervical lymph nodes in PTC patients [n (%)]

病理结果	FNAC		FNA-Tg		两者联合	
	阳性	阴性	阳性	阴性	阳性	阴性
阳性	66(81.48)	15(18.52)	75(92.59)	6(7.41)	78(96.30)	3(3.70)
阴性	14(14.74)	81(85.26)	6(6.32)	89(93.68)	4(4.21)	91(95.79)
合计	80(45.45)	96(54.55)	81(46.02)	95(53.98)	82(46.59)	94(53.41)

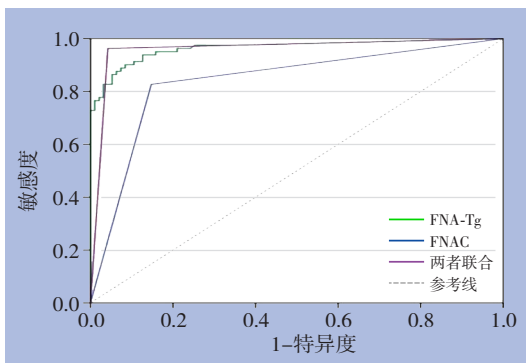


图 2 FNA-Tg、FNAC 及两者联合诊断 PTC 颈部淋巴结转移的 ROC 曲线

Figure 2 ROC curves of FNA-Tg, FNAC and their combination in diagnosis of cervical lymph node metastasis of PTC

2.3 FNAC 及 FNA-Tg 诊断效能

在 81 枚转移淋巴结中, FNAC 检出 66 枚, 15 枚出现假阴性, FNA-Tg 则检出 75 枚, 6 枚为假阴性, 两者联合应用时则检出 78 枚, 3 枚假阴性; 在 95 枚非转移淋巴结中, FNAC 诊断正确 81 枚, FNA-Tg 诊断正确 89, 两者联合时诊断正确 91 枚。FNAC 及 FNA-Tg 的诊断敏感度、特异度、准确性、阳性预测值及阴性预测值分别为 81.48%、85.26%、83.52%、82.50%、84.38% 及 92.59%、93.68%、93.18%、92.59%、93.68%; FNAC 与 FNA-Tg 联合应用时分别为 96.30%、95.79%、96.02%、95.12%、96.81%。FNA-Tg 诊断指标均高于 FNAC, 两者在敏感度、准确性及阴性预测值方面的差异有统计学意义 ($\chi^2=4.432$, $P=0.035$; $\chi^2=7.798$, $P=0.005$; $\chi^2=4.228$, $P=0.040$), 在特异度、阳性预测值方面差异无统计学意义 ($\chi^2=3.576$, $P=0.059$; $\chi^2=3.768$, $P=0.052$) (表 2)。

表 2 FNAC、FNA-Tg 及两者联合对 PTC 颈部淋巴结转移的诊断效能比较 (%)

Table 2 Comparison of diagnostic performance of FNAC, FNA-Tg, and their combination in detecting cervical lymph node metastasis in PTC (%)

检查方法	敏感度	特异度	准确性	阳性预测值	阴性预测值
FNAC	81.48	85.26	83.52	82.50	84.38
FNA-Tg	92.59	93.68	93.18	92.59	93.68
两者联合	96.30	95.79	96.02	95.12	96.81

3 讨论

PTC 是起源于甲状腺滤泡上皮细胞的恶性肿瘤, 约占甲状腺癌总数的 95%, 早期发生颈部淋巴结转移是 PTC 的特点, 也是影响 PTC 预后的重要因素, 淋巴结转移与否将影响手术方式的制定及淋巴结清扫范围^[14-16]。FNAC 是目前术前诊断颈部淋巴结转移的常用方法, 但临床工作中, 由于病理医师的经验和技术、穿刺物中细胞数量不足、淋巴结囊变坏死及淋巴结微转移等均可影响诊断准确性, 样本量不足和假阴性率分别为 5%~20% 和 6%~8%^[17]。越来越多研究^[18-21]表明测定 FNA-Tg 对淋巴结转移的诊断具有较高的诊断价值, 本文研究还得出 FNA-Tg 对 PTC 患者颈部淋巴结转移的诊断具有较高的诊断效能。

血清 Tg 是一种相对分子量接近 660 000 的糖蛋白, 是由分化良好的甲状腺滤泡细胞产生的特异分子。健康个体的血清中可检测到少量 Tg, 其在血清中浓度与甲状腺体积大小相关, 每克甲状腺组织的 Tg 浓度在 0.5~1.0 mg/L, 若 Tg 在非甲状腺组织中 (如淋巴结) 中异常表达, 可作为 DTC 转移的证据^[22-24]。

本研究中通过对两组血清 Tg 的测定结果显示

转移组血清Tg略高于非转移组,但两者差异无统计学意义($Z=1.878$, $P=0.062$),主要是两组患者均是术前病例,均存在正常甲状腺组织,所以其血清Tg数值大多数处于正常值水平,个别患者可能存在广泛的转移导致其血清Tg明显增高,两者差异无统计学意义,说明依据术前血清Tg来鉴别PTC患者是否存在淋巴结转移诊断价值有限。本研究显示转移组FNA-Tg中位数500(142.56~500)ng/mL,明显高于非转移组FNA-Tg中位数0.10(0.10~0.29)ng/mL,两组间FNA-Tg差异有统计学意义($Z=10.981$, $P<0.001$),其ROC曲线AUC为0.964(95% CI=0.937~0.992, $P<0.001$),具有较高的诊断效能,最佳诊断阈值为4.79 ng/mL,研究结论提示在临床中可以采用FNA-Tg数值高低来鉴别转移性淋巴结,这与以前的研究^[25-26]结果一致。

目前临床上判断PTC患者颈部淋巴结转移常用的为超声引导下FNAC,其应用广泛,是目前术前颈部淋巴结唯一的病理学诊断工具,诊断效能较高,本研究结论显示FNAC的诊断敏感度、特异度、准确性、阳性预测值及阴性预测值分别为81.48%、85.26%、83.52%、82.50%、84.38%,但其中也存在一定的不足,例如转移性淋巴结体积较小、淋巴结囊性变、穿刺物中诊断细胞数不足、涂片质量不高、病理医师的经验技术等,均可影响诊断准确性。近年来,研究者^[27-28]发现FNA-Tg检测在术前对PTC患者颈部淋巴结转移的诊断具有较高的临床价值,本研究得出的结论是,FNA-Tg检测对PTC患者颈部淋巴结转移的诊断具有较高的诊断效能,其诊断敏感度、特异度、准确性、阳性预测值及阴性预测值分别为92.59%、93.68%、93.18%、92.59%、93.68%,具有较高的诊断效能,与以往研究^[29-30]大致一致。

FNA-Tg检测方法操作简便,在FNAC的同时不会造成额外的创伤,并且对病理细胞学诊断医师的专业水平依赖性小,在ATA及欧洲甲状腺协会(European Thyroid Association, ETA)等指南中均推荐FNA-Tg检测作为超声引导下FNAC诊断PTC颈部淋巴结转移的有效补充手段,尤其是PTC术后随访方面,所以,在进行FNAC的同时,可同时进行FNA-Tg检测。本研究结论显示FNA-Tg诊断效能比FNAC还要高,两者在敏感度、准确性及阴性预测值方面存在明显差异(均 $P<0.05$),特异度和阳性预测值差异虽无统计学意义,但FNA-Tg均高于FNAC。

在FNAC检查中,诊断正确81枚转移淋巴结中的66枚,在出现的假阴性15枚淋巴结中,6枚出现了囊变坏死区,在细胞涂片中只见到了囊液及吞噬细胞,未见明确肿瘤细胞,5枚淋巴结体积较小,长径 <8 mm,体积较小并可能受患者紧张伴随吞咽动作导致取材部位不精准,余下4个病理图片背景中存在大量血细胞受到影响导致漏诊;而在95枚非转移淋巴结中,诊断正确81枚,误诊了14枚淋巴结,可能是取材不理想或受到病理细胞学诊断医师的技术经验水平影响。

在FNA-Tg检测中,81枚转移淋巴结诊断正确75枚,比FNAC检测出阳性例数增多,主要是因为FNA-Tg检测为客观检测,不受细胞形态的限制,可避免病理诊断医师的主观性影响,并可检测出在FNAC中可能漏诊的伴有囊性变的转移性淋巴结;FNA-Tg检测中6枚淋巴结出现了假阴性,在这6枚淋巴结中有5枚体积较小,长径 <8 mm,可能是由于淋巴结体积小导致穿刺取材部位不精准导致,而在95枚非转移淋巴结中,89枚诊断正确,误诊了6枚淋巴结,其中有5枚穿刺标准不佳,在穿刺过程中可能受到血清Tg的干扰,导致Tg检测数值增高。两者联合应用诊断敏感度有所提升,在FNA-Tg基础上增加了3枚FNAC中阴性的淋巴结,敏感度由81.48%提升到96.30%。

将FNAC和FNA-Tg检测联合应用时,其诊断效能较两者单独应用时明显增高,其诊断敏感度、特异度、准确性、阳性预测值及阴性预测值分别为96.30%、95.79%、96.02%、95.12%、96.81%,与FNAC进行统计学比较,诊断指标均有显著性差异(均 $P<0.05$),与FNA-Tg比较,差异虽无统计学意义(均 $P>0.05$),但较FNA-Tg均有所进一步提高,提示在临床中,应将两种检测方法联合应用,以达到最佳诊断效能。

综上所述,超声引导下FNAC在PTC颈部淋巴结转移诊断中具有一定诊断价值,但其存在一定不足,而FNA-Tg检测是一种客观诊断方式,并未增加患者额外创伤、又同时避免了一些病理医师主观因素影响,从而可提高诊断准确性,其ROC曲线AUC为0.964具有较高的诊断效能,最佳诊断阈值为4.79 ng/mL。FNA-Tg对诊断PTC颈部淋巴结转移具有较高的诊断价值,且高于FNAC,临床工作中将两者联合应用可进一步提高PTC患者颈部淋巴结转移的诊断价值。

利益冲突：所有作者均声明不存在利益冲突。

作者贡献声明：王亚楠提出研究方向,负责文献的收集,文章的起草与撰写;张欢、欧阳向柳、韩云霞负责文章的构思,回顾性整理病例资料,绘制图表;刘丽云对论文初稿及英文摘要进行修订;郑立春对论文终稿进行审校,负责文章的质量控制。

参考文献

- [1] Bray F, Ferlay J, Soerjomataram I, et al. Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries[J]. *CA Cancer J Clin*, 2018,68(6):394-424. doi:10.3322/caac.21492.
- [2] 郑荣寿,孙可欣,张思维,等. 2015年中国恶性肿瘤流行情况分析[J]. *中华肿瘤杂志*, 2019, 41(1):19-28. doi:10.3760/cma.j.issn.0253-3766.2019.01.008.
Zheng RS, Sun KX, Zhang SW, et al. Report of cancer epidemiology in China, 2015[J]. *Chinese Journal of Oncology*, 2019, 41(1):19-28. doi:10.3760/cma.j.issn.0253-3766.2019.01.008.
- [3] 陈怡如,雷亚丽,邹联洪,等. 儿童及青少年甲状腺癌的临床特征与预后分析[J]. *中国普通外科杂志*, 2022, 31(5):608-618. doi:10.7659/j.issn.1005-6947.2022.05.006.
Chen YR, Lei YL, Zou LH, et al. Analysis of clinical characteristics and prognosis of thyroid cancer in children and adolescents[J]. *China Journal of General Surgery*, 2022, 31(5): 608-618. doi:10.7659/j.issn.1005-6947.2022.05.006.
- [4] Amit M, Tam S, Boonsripitayanon M, et al. Association of lymph node density with survival of patients with papillary thyroid cancer[J]. *JAMA Otolaryngol Head Neck Surg*, 2018, 144(2): 108-114. doi:10.1001/jamaoto.2017.2416.
- [5] Lim H, Devesa SS, Sosa JA, et al. Trends in thyroid cancer incidence and mortality in the United States, 1974-2013[J]. *JAMA*, 2017, 317(13):1338-1348. doi:10.1001/jama.2017.2719.
- [6] 孔令欣,王照华,殷文斌,等. 甲状腺微小乳头状癌侧颈淋巴结转移相关危险因素与预测指标分析[J]. *中国普通外科杂志*, 2021, 30(5):537-542. doi:10.7659/j.issn.1005-6947.2021.05.005.
Kong LX, Wang ZH, Yin WB, et al. Analysis of risk factors and predictive variables for lateral cervical lymph node metastasis in papillary thyroid microcarcinoma[J]. *China Journal of General Surgery*, 2021, 30(5): 537-542. doi:10.7659/j.issn.1005-6947.2021.05.005.
- [7] 周武琳,程晓明,吕俊远,等. 基于FNAB的分子检测技术在甲状腺结节诊断中的研究进展[J]. *中国普通外科杂志*, 2021, 30(5): 613-621. doi:10.7659/j.issn.1005-6947.2021.05.015.
Zhou WL, Cheng XM, Lü JY, et al. Research progress of molecular detection technologies based on FNAB in diagnosis of thyroid nodules[J]. *China Journal of General Surgery*, 2021, 30(5): 613-621. doi:10.7659/j.issn.1005-6947.2021.05.015.
- [8] Zhao H, Wang Y, Wang MJ, et al. Influence of presence/absence of thyroid gland on the cutoff value for thyroglobulin in lymph-node aspiration to detect metastatic papillary thyroid carcinoma[J]. *BMC Cancer*, 2017, 17(1):296. doi:10.1186/s12885-017-3296-3.
- [9] Song YT, Xu GH, Wang TX, et al. Lateral neck multilevel fine-needle aspiration cytology and thyroglobulin estimation in papillary thyroid carcinoma[J]. *Laryngoscope Investig Otolaryngol*, 2021, 6(3):570-575. doi:10.1002/liv.2.570.
- [10] Song YT, Wang JX, Zhu YL, et al. Is thyroglobulin detection in fine-needle aspirates useful for the diagnosis of central neck metastatic papillary thyroid cancer?[J]. *Endocr Connect*, 2022, 11(12):e220353. doi:10.1530/EC-22-0353.
- [11] Liu NX, Tang LN, Chen YJ, et al. A Combination of Contrast-Enhanced Ultrasound and Thyroglobulin Level in Fine-Needle Aspirates Improves Diagnostic Accuracy for Metastatic Lymph Nodes of Papillary Thyroid Carcinoma [J]. *J Ultrasound Med*, 2022, 41(10): 2431-2443. doi:10.1002/jum.15926.
- [12] Wang Y, Duan Y, Li H, et al. Detection of thyroglobulin in fine-needle aspiration for diagnosis of metastatic lateral cervical lymph nodes in papillary thyroid carcinoma: a retrospective study[J]. *Front Oncol*, 2022, 12:909723. doi:10.3389/fonc.2022.909723.
- [13] Haugen BR. 2015 American Thyroid Association Management Guidelines for Adult Patients with Thyroid Nodules and Differentiated Thyroid Cancer: what is new and what has changed? [J]. *Cancer*, 2017, 123(3): 372-381. doi:10.1002/cncr.30360.
- [14] 王源源,吴国洋,罗晔哲,等. 经胸经口联合入路腔镜甲状腺癌颈侧区淋巴结清扫术临床应用[J]. *中国普通外科杂志*, 2022, 31(11):1437-1444. doi:10.7659/j.issn.1005-6947.2022.11.005.
Wang YY, Wu GY, Luo YZ, et al. Application of endoscopic thyroidectomy plus lateral neck dissection via breast approach combined with transoral approach[J]. *China Journal of General Surgery*, 2022, 31(11): 1437-1444. doi:10.7659/j.issn.1005-6947.2022.11.005.
- [15] 帅师,付言涛. cN0期甲状腺乳头状癌中央组淋巴结预防性清扫的研究进展[J]. *中国普通外科杂志*, 2020, 29(11):1376-1384. doi:10.7659/j.issn.1005-6947.2020.11.012.
Shi S, Fu YT. Research progress of prophylactic central lymph node dissection in cN0 papillary thyroid cancer[J]. *China Journal of General Surgery*, 2020, 29(11): 1376-1384. doi:10.7659/j.issn.1005-6947.2020.11.012.
- [16] Jia X, Wang Y, Liu Y, et al. Thyroglobulin Measurement Through Fine-Needle Aspiration for Optimizing Neck Node Dissection in Papillary Thyroid Cancer [J]. *Ann Surg Oncol*, 2022, 29(1):88-96. doi:10.1245/s10434-021-10549-2.
- [17] Xu YX, Wu DP, Wu WT, et al. Diagnostic value of cytology, thyroglobulin, and combination of them in fine-needle aspiration of metastatic lymph nodes in patients with differentiated thyroid cancer: a systematic review and network meta-analysis[J]. *Medicine (Baltimore)*, 2019, 98(45): e17859. doi:10.1097/

- MD.000000000017859.
- [18] Zhu XH, Zhou JN, Qian YY, et al. Diagnostic values of thyroglobulin in lymph node fine-needle aspiration washout: a systematic review and meta-analysis diagnostic values of FNA-Tg[J]. *Endocr J*, 2020, 67(2):113-123. doi: 10.1507/endocrj.EJ18-0558.
- [19] Wu XL, Liu Y, Li KJ, et al. Predictive value of FNA-tg and TgAb in cervical lymph node metastasis of papillary thyroid carcinoma[J]. *Technol Cancer Res Treat*, 2022, 21: 15330338221127605. doi: 10.1177/15330338221127605.
- [20] Sun JJ, Li PP, Chen X, et al. The influence of thyroid status, serum Tg, TSH, and TgAb on FNA-Tg in cervical metastatic lymph nodes of papillary thyroid carcinoma[J]. *Laryngoscope Investig Otolaryngol*, 2022, 7(1):274-282. doi: 10.1002/liv.2.717.
- [21] Jia X, Tao RY, Yang Y, et al. ASO author reflection: optimizing lateral neck dissection extent of PTC by FNA-tg[J]. *Ann Surg Oncol*, 2022, 29(1):97-98. doi: 10.1245/s10434-021-10636-4.
- [22] Lim JH, Kim DW, Park JY, et al. Ultrasonography, cytology, and thyroglobulin measurement results of cervical nodal metastasis in patients with unclear papillary thyroid carcinoma[J]. *Front Endocrinol (Lausanne)*, 2019, 10: 395. doi: 10.3389/fendo.2019.00395.
- [23] 石灿, 彭松, 梁琪. 能谱CT及其联合甲状腺球蛋白检测对良恶性甲状腺结节的诊断价值[J]. *中国普通外科杂志*, 2021, 30(11): 1359-1366. doi: 10.7659/j.issn.1005-6947.2021.11.012.
- Shi C, Peng S, Liang Q. Diagnostic values of spectral CT and its combination with thyroglobulin detection for benign or malignant thyroid nodules[J]. *China Journal of General Surgery*, 2021, 30(11): 1359-1366. doi: 10.7659/j.issn.1005-6947.2021.11.012.
- [24] Blažeković I, Romić M, Bosak Butković M, et al. Thyroglobulin measurement in needle aspiration for detection of recurrences and neck metastases in patients with differentiated thyroid carcinoma: significance of anti-tg antibodies[J]. *Acta Clin Croat*, 2020, 59 (Suppl 1):9-17. doi: 10.20471/acc.2020.59.s1.01.
- [25] 刘娜香, 唐丽娜, 沈友洪, 等. 超声引导下细针抽吸活检联合洗脱液测定甲状腺球蛋白诊断甲状腺乳头状癌侧颈部淋巴结转移[J]. *中国介入影像与治疗学*, 2019, 16(9):527-530. doi: 10.13929/j.1672-8475.201903005.
- Liu NX, Tang LN, Shen YH, et al. Ultrasound-guided fine-needle aspiration biopsy combined with washout fluid thyroglobulin detection in diagnosis of lateral neck lymph nodes metastasis of papillary thyroid carcinoma[J]. *Chinese Journal of Interventional Imaging and Therapy*, 2019, 16(9):527-530. doi: 10.13929/j.1672-8475.201903005.
- [26] 杨薇, 卢漫, 王朝晖, 等. 超声联合FNA-Tg检测诊断甲状腺乳头状癌侧颈部淋巴结转移的临床价值[J]. *肿瘤预防与治疗*, 2021, 34(9):843-848. doi:10.3969/j.issn.1674-0904.2021.09.010.
- Yang W, Lu M, Wang ZH, et al. Clinical value of ultrasound combined with FNA-tg in the diagnosis of lateral cervical lymph node metastasis in papillary thyroid carcinoma[J]. *Journal of Cancer Control and Treatment*, 2021, 34(9): 843-848. doi: 10.3969/j.issn.1674-0904.2021.09.010.
- [27] 纪丽丽, 姜双全, 李守强, 等. 穿刺洗脱液甲状腺球蛋白测定在诊断甲状腺乳头状癌转移淋巴结中的应用[J]. *中华超声影像学杂志*, 2019, 28(4): 313-317. doi: 10.3760/cma.j.issn.1004-4477.2019.04.007.
- Ji LL, Jiang SQ, Li SQ, et al. Application of thyroglobulin measurement in fine-needle aspiration for detecting lymph node metastasis in papillary thyroid carcinoma[J]. *Chinese Journal of Ultrasonography*, 2019, 28(4): 313-317. doi: 10.3760/cma.j.issn.1004-4477.2019.04.007.
- [28] 刘娜香, 唐丽娜, 沈友洪, 等. 超声造影联合穿刺洗脱液甲状腺球蛋白测定在诊断甲状腺乳头状癌侧颈部转移淋巴结中的应用价值[J]. *中华超声影像学杂志*, 2020, 29(12):1060-1066. doi: 10.3760/cma.j.cn131148-20200806-00637.
- Liu NX, Tang LN, Shen YH, et al. Values of contrast-enhanced ultrasound and thyroglobulin measurement in fine-needle aspiration for detecting lateral cervical lymph node metastasis of papillary thyroid carcinoma[J]. *Chinese Journal of Ultrasonography*, 2020, 29(12):1060-1066. doi: 10.3760/cma.j.cn131148-20200806-00637.
- [29] 曹亚, 张辉, 孟林, 等. 彩色超声、FNA-C、FNA-Tg在诊断甲状腺乳头状癌(PTC)颈部淋巴结转移中的价值[J]. *昆明医科大学学报*, 2021, 42(11):105-110. doi:10.12259/j.issn.2095-610X.S20211119.
- Cao Y, Zhang H, Meng L, et al. Value of Color Doppler Ultrasonography, Fine Needle Aspiration Cytology, and the Level of Thyroglobulin in the Diagnosis of Cervical Lymph Node Metastasis of Papillary Thyroid Carcinoma[J]. *Journal of Kunming Medical University*, 2021, 42(11): 105-110. doi: 10.12259/j.issn.2095-610X.S20211119.
- [30] 李偲育, 王茜, 范公林, 等. 基于超声与细针穿刺洗脱液甲状腺球蛋白检测建立甲状腺乳头状癌颈部淋巴结转移的预测模型[J]. *中华超声影像学杂志*, 2020, 29(2):131-137. doi: 10.3760/cma.j.issn.1004-4477.2020.02.006.
- Li YY, Wang Q, Fan GL, et al. Predictive model for cervical lymph node metastasis of papillary thyroid carcinoma based on ultrasound and thyroglobulin in fine-needle aspirate fluid detection[J]. *Chinese Journal of Ultrasonography*, 2020, 29(2): 131-137. doi: 10.3760/cma.j.issn.1004-4477.2020.02.006.

(本文编辑 宋涛)

本文引用格式:王亚楠,张欢,欧阳向柳,等.细针穿刺洗脱液甲状腺球蛋白检测对甲状腺乳头状癌颈部淋巴结转移的诊断价值[J].*中国普通外科杂志*, 2023, 32(5): 690-697. doi: 10.7659/j.issn.1005-6947.2023.05.008

Cite this article as: Wang YN, Zhang H, Ouyang XL, et al. Diagnostic value of thyroglobulin detection in washout fluid of fine-needle aspiration biopsy for cervical lymph node metastasis in papillary thyroid carcinoma[J]. *Chin J Gen Surg*, 2023, 32(5): 690-697. doi: 10.7659/j.issn.1005-6947.2023.05.008