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甲状腺微小癌颈部淋巴结转移超声特征及淋巴结转移危险因素 Logistic 回归分析*

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摘要 目的:观察甲状腺微小癌(TMC)颈部淋巴结转移的超声特征,分析TMC发生淋巴结转移的危险因素。方法:选择2013年5月~2017年6月经本院手术病理证实的TMC患者197例为研究对象,其中伴颈部淋巴结转移的60例为转移组,无颈部淋巴结转移的137例为非转移组,观察其超声图像特征,采用单因素和多因素Logistic回归分析法分析颈部淋巴结转移的独立危险因素。结果:197例TMC患者共224个病灶,术后病理证实60例(67个病灶)有颈部淋巴结转移,137例(157个病灶)无颈部淋巴结转移,以术后病理诊断结果为金标准,超声诊断TMC颈部淋巴结转移的敏感性为16.67%(10/60),特异性为94.89%(130/137),准确性为71.07%(140/197),阳性预测值为58.82%(10/17),阴性预测值为72.22%(130/180)。单因素分析显示TMC颈部淋巴结转移与年龄、肿瘤最大径、肿瘤形态、钙化情况有关($P<0.05$)。多因素Logistic回归分析显示,年龄 ≤ 50 岁、肿瘤形态不规则、微钙化是TMC颈部淋巴结转移的独立危险因素($P<0.05$)。结论:超声诊断TMC颈部淋巴结转移的敏感性低,TMC颈部淋巴结转移与年龄、肿瘤形态和钙化情况有关。

关键词: 甲状腺微小癌;颈部淋巴结转移;超声特征;危险因素;Logistic回归分析

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Thyroid Microcarcinoma: Ultrasonography Characteristics of Neck Lymph Node Metastases and Logistic Regression Analysis of Its Risk Factors*

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ABSTRACT Objective: To observe the ultrasonography characteristics of neck lymph node metastases in thyroid microcarcinoma (TMC), and analyze the risk factors of lymph node metastasis in TMC. **Methods:** A total of 197 TMC patients, who were proved by the operation and pathology in China Meitan General Hospital from May 2013 to June 2017, were chosen as subjects. Among them, 60 cases with neck lymph node metastasis were chosen as transfer group and 137 cases without neck lymph node metastasis, as non transfer group. The ultrasonic image characteristics of the two groups were observed. Univariate and multivariate Logistic regression analysis were used to analyze the independent risk factors of neck lymph node metastasis. **Results:** There were 224 lesions in 197 patients with TMC. There were 60 cases (67 lesions) with neck lymph node metastasis and 137 cases (157 lesions) without neck lymph node metastasis confirmed by the postoperative pathology. As the gold standard of the postoperative pathological diagnosis, the sensitivity of ultrasonic diagnosis with cervical lymph node metastases in TMC was 16.67% (10/60), the specificity was 94.89% (130/137), the accuracy was 71.07% (140/197), the positive predictive value was 58.82% (10/17), the negative predictive value was 72.22% (130/180). Univariate analysis showed that neck lymph node metastasis in TMC was related to patients' age, maximum diameter of tumor, tumor shape and calcification ($P<0.05$). Multivariate Logistic regression analysis showed that the age ≤ 50 years old, irregular shape and microcalcification were the independent risk factors of neck lymph node metastases in TMC ($P<0.05$). **Conclusion:** The sensitivity of ultrasonic diagnosis in neck lymph node metastasis of TMC is low, and neck lymph node metastasis in TMC is related to age, morphology of tumor and calcification.

Key words: Thyroid microcarcinoma; Neck lymph node metastases; Ultrasonography characteristics; Risk factors; Logistic regression analysis

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前言

甲状腺微小癌(Thyroid microcarcinoma, TMC)即最大直径 ≤ 1.0 cm的甲状腺癌,是临床上较为常见的甲状腺恶性肿瘤

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瘤,近年来其发病率呈上升的趋势^[1]。临床上多采用手术方式对TMC进行治疗,然而关于术中对颈侧淋巴结是否进行清扫尚存在一定的争议^[2,3]。TMC手术治疗中,是否进行淋巴结清扫的关键在于是否有淋巴结转移,若有颈部淋巴结转移,则进行进一步的淋巴结清扫是提高疗效及保障患者术后安全的关键环节^[4,5]。超声检查作为甲状腺癌的术前检查手段,能够为术前评估癌细胞转移情况提供丰富的信息,然而由于超声检查受肿瘤直径大小、转移程度等因素的影响,术前超声检查诊断其颈部淋巴结转移的敏感度较低,相关文献报道敏感度仅为17.3%~23.0%^[6-8]。因而术前单纯的超声诊断TMC颈部淋巴结转移的价值有限,有待进一步研究。本文通过观察TMC的超声图像特征,进一步探究其超声图像特征及病理资料与颈部淋巴结转移的相关性,探明其相关因素,以期为该病的早期诊断、制定具体手术方案提供参考。

1 资料和方法

1.1 一般资料

选择2013年5月~2017年6月经本院手术病理证实的TMC患者197例作为研究对象。纳入标准:(1)术前经甲状腺常规、超声、CT等检查明确诊断,术中留取组织标本,术后病理组织学确诊^[9];(2)肿瘤最大直径<1.0 cm;(3)临床资料完整。排除标准:(1)合并内分泌系统及头颈部其他肿瘤者;(2)病理诊断结果不明确者;(3)超声图像质量不理想者。197例TMC患者中,男50例,女147例;年龄20~81岁,平均(49.37±9.78)岁;病理分型:乳头状癌178例,滤泡状癌18例,髓样癌1例;所有患者均为未分化型癌;单发灶178例,多发灶19例(其中2个病灶的12例,3个病灶的6例,4个病灶的1例);临床分期:根据第六版TNM分期标准,I期44例,II期58例,III期61例,IV期34例。本研究经本院伦理委员会审核批准。

1.2 方法

1.2.1 超声检查 所有患者术前均采用HITACHI HI VISION AVIUS全数字化彩色超声诊断仪和Philips EnVisor C型彩色多普勒超声诊断仪进行检查,探头频率5~12 MHz,患者取仰卧位,充分暴露颈前部,首先常规探查甲状腺及颈部淋巴结情况,探查时注意探头不要对皮肤进行加压以免压迫淋巴血管造成血供减少,观察甲状腺结节回声、纵横比、边界、微钙化及血供情况,观察颈部淋巴结回声、长短径比、淋巴门结构是否消失、微钙化、血供、是否伴液化等情况,再仔细探查可疑病区,发现病灶仔细观察病灶大小、数目、所处位置、纵横比(病灶和皮肤的垂直最大径与病灶和皮肤的平行最大径之比)、回声情况、边界及形态、内部结构(无囊性、囊性<50%则实性为主、囊性≥50%则囊性为主)、钙化情况(无钙化、粗钙化和微钙化)、病灶

与包膜接触面积(病灶边界与甲状腺包膜的接触面积占病灶面积的积分比,分为0%、1%~25%、26%~50%和>50%四个肌壁)、血供程度(按照Adler分级法^[10]分为0级、1级、2级和3级)、有无后方衰减、有无声晕等。超声图像均由超声科具有至少5年工作经验的高级职称医师综合分析进行诊断。

1.2.2 病理诊断 术前根据甲状腺常规、超声、CT等检查(若无法确诊则在超声引导下行细针穿刺细胞学诊断)进行手术,其中行甲状腺全切术的53例,甲状腺次全切除术144例,术中留取组织标本送检,常规石蜡包埋切片,HE染色后由2名至少具有5年工作经验的病理医师观察作出明确诊断。

1.3 观察指标

(1)观察超声对TMC颈部淋巴结转移的诊断情况:以术后病理诊断结果为金标准,计算超声诊断TMC颈部淋巴结转移的敏感性、特异性、准确性、阳性预测值、阴性预测值。TMC颈部淋巴结转移的超声诊断标准^[10]:①淋巴结内出现微小钙化;②淋巴结内出现液化或囊性区;③淋巴结长短径比较<2;④淋巴门消失或淋巴结结构不清;⑤出现多发团、片状高回声区;⑥血供丰富或较丰富。满足①、②中的其中一项或满足③~⑥中的任意2项即可诊断为TMC颈部淋巴结转移。(2)TMC颈部淋巴结转移的相关因素单因素分析:根据病理诊断结果,比较有无颈部淋巴结转移患者的临床资料和超声特征的差异,包括性别、年龄(以50岁为界)、肿瘤最大径(以0.5 cm为界)、纵横径比、病灶数、病灶与包膜接触面积、回声情况(分为高回声、等回声、低回声)、边界和形态、病灶位置、内部结构、钙化情况、血供程度、有无后方衰减、有无声晕等。

1.4 统计学方法

本研究所有数据均采用SPSS18.0软件进行统计分析,临床资料及超声特征表现采用计数资料表示,用率(%)描述,转移组与非转移组比较的单因素分析采用 χ^2 检验,TMC颈部淋巴结转移的危险因素采用多因素Logistic回归分析,以 $P<0.05$ 为差异有统计学意义。

2 结果

2.1 超声诊断结果与术后病理诊断结果比较

197例TMC患者共224个病灶,术后病理诊断结果提示,60例(共67个病灶)有颈部淋巴结转移,137例(共157个病灶)无颈部淋巴结转移。超声检查有颈部淋巴结转移17例,其中包括7例假阳性;无颈部淋巴结转移180例,其中包括50例假阴性;以术后病理诊断结果为金标准,超声诊断TMC颈部淋巴结转移的敏感性为16.67%(10/60),特异性为94.89%(130/137),准确性为71.07%(140/197),阳性预测值为58.82%(10/17),阴性预测值为72.22%(130/180)。见表1。

表1 TMC颈部淋巴结转移的超声诊断结果与术后病理结果比较

Table 1 Comparison of ultrasonic diagnosis results and postoperative pathological findings of cervical lymph node metastasis in TMC

		Postoperative pathology		Total
		+	-	
Preoperative ultrasound	+	10	7	17
	-	50	130	180
	Total	60	137	197

2.2 TMC 颈部淋巴结转移相关因素单因素分析

单因素分析结果显示,TMC 颈部淋巴结转移与性别、病灶数、纵横径比、病灶与包膜接触面积、回声情况、肿瘤位置、肿瘤

边界、内部结构、血供程度、有无声晕和有无后方衰减无关($P>0.05$),与患者的年龄、肿瘤最大径、肿瘤形态、钙化情况有关($P<0.05$),见表 2。

表 2 TMC 颈部淋巴结转移相关因素单因素分析

Table 2 Single factor analysis of related factors of cervical lymph node metastasis in TMC

Factors		n	Cervical lymph node metastasis[n(%)]		χ^2	P
			Yes(n=60 or 67)	No(n=137 or 157)		
Sex*	Male	50	13(26.00)	37(74.00)	2.173	0.207
	Female	147	47(31.97)	100(68.03)		
Age*	≤ 50 years	138	48(34.78)	90(65.22)	4.071	0.044
	> 50 years	59	12(20.34)	47(79.66)	0.013	0.911
Lesion number*	Single shot	178	54(30.34)	124(69.66)	4.717	0.030
	Multiple	19	6(31.58)	13(68.42)		
Maximum diameter of tumor	≤ 0.5 cm	43	7(16.28)	36(83.72)	0.856	0.355
	>0.5 cm	181	60(33.15)	121(66.85)		
Aspect ratio	< 1	45	16(35.56)	29(64.44)	2.481	0.189
	≥ 1	179	51(28.49)	128(71.51)		
Contact area between lesion and capsule	0%	85	22(25.88)	63(74.12)	2.007	0.221
	1%~25%	113	34(30.09)	79(69.91)		
	26%~50%	26	11(42.31)	15(57.69)		
	$> 50\%$	0	0(0.00)	0(0.00)		
Echo condition	High echo	223	66(29.60)	157(70.40)	0.944	0.805
	Equal echo	1	1(100.00)	0(0.00)		
	Low echo	0	0(0.00)	0(0.00)		
Tumor location	Upper	54	14(25.93)	40(74.07)	2.562	0.109
	Middle	90	23(25.56)	67(74.44)		
	Lower	71	28(39.44)	43(60.56)		
	Isthmus	9	2(22.22)	7(77.78)		
Tumor border	Clear	56	12(21.43)	44(78.57)	6.821	0.009
	Blurring	168	55(32.74)	113(67.26)		
Tumor morphology	Regular	56	9(16.07)	47(83.93)	2.114	0.218
	Irregular	168	58(34.52)	110(65.48)		
Internal structure	Non cystic	223	66(29.60)	157(70.40)	0.853	0.847
	Cystic dominant	0	0(0.00)	0(0.00)		
	Solid based	1	1(100.00)	0(0.00)		
Blood supply degree	Rank 0	80	21(26.25)	59(73.75)	0.047	0.829
	Rank 1	58	19(32.76)	39(67.24)		
	Rank 2	54	16(29.63)	38(70.37)		
	Rank 3	32	11(34.38)	21(65.62)		
Acoustic halo	Yes	4	1(25.00)	3(75.00)	0.836	0.361
	No	220	66(30.00)	154(70.00)		
Backward attenuation	Yes	12	5(41.67)	7(58.33)	8.497	0.003
	No	212	62(29.25)	150(70.75)		
Calcification	No calcification	111	27(24.32)	84(75.68)	6.821	0.009
	Microcalcification	88	34(38.64)	54(61.36)		
	Coarse calcification	25	6(24.00)	19(76.00)		

2.3 TMC 颈部淋巴结转移的危险因素 Logistic 回归分析

以颈部淋巴结转移情况为因变量(转移=1,未转移=0),以表2中的有统计学差异的指标为自变量进行多因素 Logistic

回归模型分析,结果显示:年龄≤50岁、肿瘤形态不规则、微钙化是 TMC 颈部淋巴结转移的独立危险因素($P<0.05$),见表3。

表3 TMC 颈部淋巴结转移的危险因素 Logistic 回归分析

Table 3 Logistic regression analysis of risk factors for cervical lymph node metastasis in TMC

Variables	β	SE	Wald	P	OR	95%CI
Age≤ 50 years	1.079	0.369	5.798	0.022	2.375	1.173~4.618
Irregular Tumor morphology	1.184	0.417	6.418	0.019	1.578	1.032~6.574
Microcalcification	1.010	0.713	12.654	0.000	4.392	2.653~15.794

Notes:* Items were calculated according to the number of cases, the rest were calculated according to the number of foci.

3 讨论

TMC 是甲状腺癌的一种亚型,其病理类型以甲状腺微小乳头状癌为主,相关研究^[11,12]报道乳头状癌占 TMC 的比例超过 85%,其他病理类型(如滤泡状癌、髓样癌等)所占的比例则较少。TMC 的临床症状和体征与甲状腺癌基本一致,但其病灶小于 1.0 cm,若不认真检查往往难以发现,近年来随着影像技术的进步,TMC 的检出率明显升高^[13,14]。TMC 患者经手术治疗后虽能获得较满意的效果(术后 10 年生存率超过 90%),但若有淋巴结转移,则术中需要进行淋巴结清扫以确保手术效果,无淋巴结转移则不建议进行淋巴结清扫,避免造成不必要的手术创伤^[15-17]。因此,术前准确判断 TMC 是否有颈部淋巴结转移对制定手术治疗方案、改善预后有重要意义。既往研究显示超声检查诊断 TMC 颈部淋巴结转移的敏感性低,本研究中术前超声诊断 TMC 颈部淋巴结转移的敏感性、特异性、准确性、阳性预测值和阴性预测值依次为 16.67%、94.89%、71.07%、58.82% 和 72.22%,敏感性和准确性均较低,其可能原因主要包括:颈部淋巴结的解剖位置较为特殊,淋巴结所处位置较深且内部结构复杂,造成声束不宜通过,从而导致超声显示不完整,无法作出准确判断导致漏诊或误诊^[18-20];TMC 颈部淋巴结转移在病理上是一个不断累积的过程,只有当转移发生到一定程度、转移的癌细胞达到一定的数量时,超声检查方能发现^[21-23];超声科医师的临床经验及对 TMC 颈部淋巴结转移的超声图像认识也可能造成影响^[24]。

单因素分析结果显示,TMC 颈部淋巴结转移与患者的性别、病灶数、纵横径比、病灶与包膜接触面积、回声情况、肿瘤位置、肿瘤边界、内部结构、血供程度、有无声晕和有无后方衰减等无明显的相关性;与患者的年龄、肿瘤最大径、肿瘤形态、钙化情况有关。多因素 Logistic 回归分析显示,年龄≤50岁、肿瘤形态不规则、微钙化是 TMC 颈部淋巴结转移的独立危险因素。谭卓等^[25]研究认为,TMC 颈部淋巴结转移与肿瘤大小、包膜侵犯、病灶位置和中央区转移等有关,有中央区淋巴结转移和肿瘤位置是独立危险因素。张剑等^[26]的研究显示,患者性别、年龄、肿瘤形态和钙化水平有关,性别、年龄和包膜侵犯是 TMC 颈部淋巴结转移的独立影响因素。而本研究显示与肿瘤最大径、病灶跟包膜的接触面积、病灶位置等无关。造成此差异的原因可能为^[27-29]:第一,样本含量差异;第二,本研究观察病灶与包膜的接触面积,而既往研究则评价是否有包膜侵犯;第三,对肿瘤位置的界定,既往研究分为上、中、下和全甲状腺,本研究分

上、中、下和峡部;第四,既往研究病例中仅为甲状腺微小乳头状癌,而本研究中包括了滤泡癌和髓样癌等其他病理类型的甲状腺微小癌。

本研究共分析了 15 个项目(其中包括 12 个超声特征项目)与 TMC 颈部淋巴结转移关系,其中仅 3 个项目是其危险因素,12 个超声特征项目中仅 2 个项目是危险因素。据此推断术前超声诊断 TMC 颈部淋巴结转移的敏感性低的原因可能与特异性特征较少有关^[30]。由此可见,术前超声诊断 TMC 颈部淋巴结转移的价值有限,建议采用超声联合同位素扫描、实验室检查等手段,并结合患者的年龄特点对其作出准确的早期诊断,若有必要可在超声引导下穿刺活检。

综上所述,年龄≤50岁、肿瘤形态不规则、病灶内微钙化是 TMC 颈部淋巴结转移的独立危险因素,观察 TMC 的肿瘤形态和病灶内钙化情况等超声特征有助于预测术前颈部淋巴结转移,但单独超声诊断的敏感性、准确性低,临床价值有限。

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