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## • 临床研究 •

# Luminal A 型和 Luminal B 型乳腺癌患者的腋窝淋巴结转移发生率及预后的比较研究 \*

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**摘要 目的:**对比 Luminal A 型和 Luminal B 型乳腺癌患者的腋窝淋巴结转移发生率及预后情况。**方法:**回顾性分析我院从 2011 年 5 月~2014 年 12 月收治的乳腺癌患者 180 例作为研究对象。将其按照临床病理类型的差异分成 Luminal A 型组 84 例与 Luminal B 型组 96 例。比较两组临床病理特征、腋窝淋巴结转移发生率、5 年复发率与生存率,比较两组患者超声学特征。**结果:**Luminal A 型组年龄 >50 岁、肿瘤大小 ≤ 2 cm、组织分级 I 级人数占比均高于 Luminal B 型组( $P<0.05$ )。Luminal A 型组腋窝淋巴结转移发生率为 13.10%(11/84),显著低于 Luminal B 型组的 39.58%(38/96)( $P<0.05$ )。Luminal A 型组和 Luminal B 型组患者的 5 年复发转移率对比差异无统计学意义 ( $P>0.05$ ),Luminal A 型组 5 年生存率为 86.90%(73/84), 高于 Luminal B 型组的 73.96%(71/96)( $P<0.05$ )。Luminal A 型组边界清晰、无钙化人数占比均高于 Luminal B 型组,而 Alder 为 III 级人数占比低于 Luminal B 型组( $P<0.05$ )。**结论:**Luminal A 型乳腺癌患者的腋窝淋巴结转移发生率低于 Luminal B 型乳腺癌患者,且两者的临床病理和超声学特征存在一定的差异,Luminal A 型乳腺癌患者的预后优于 Luminal B 型。

**关键词:**乳腺癌;Luminal A 型;Luminal B 型;腋窝淋巴结;转移;预后

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## A Comparative Study on the Incidence and Prognosis of Axillary Lymph Node Metastasis in Luminal Type A and Luminal Type B Breast Cancer Patients\*

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**ABSTRACT Objective:** To compare the incidence and prognosis of axillary lymph node metastasis in Luminal type A and Luminal type B breast cancer patients. **Methods:** A retrospective analysis was performed on 180 cases of breast cancer who were admitted to our hospital from May 2011 to December 2014 as an object of study. According to the differences of clinicopathological types, they were divided into two groups: 84 patients in Luminal type A group and 96 patients in Luminal type B group. The clinicopathological features, incidence of axillary lymph node metastasis, 5-year recurrence rate and survival rate of the two groups were compared. In addition, the ultrasonic characteristics of the two groups of patients were compared. **Results:** Luminal type A group age > 50 years old, and tumor size ≤ 2 cm, organize class I number proportion were significantly higher than that of Luminal type B group ( $P<0.05$ ). The incidence of axillary lymph node metastasis in Luminal type A group was 13.10% (11/84), which was significantly lower than 39.58% (38/96) in Luminal type B group ( $P<0.05$ ). There were no significant differences in 5-year recurrence and metastasis rate between Luminal type A group and Luminal type B group ( $P>0.05$ ). The 5-year survival rate in Luminal type A group was 86.90% (73/84), which was significantly higher than 73.96% (71/96) in Luminal type B group ( $P<0.05$ ). The boundary clear, no calcification in Luminal type A group were higher than those in Luminal type B group, and Alder III grade number proportion was lower than that in Luminal type B group ( $P<0.05$ ). **Conclusion:** The incidence of axillary lymph node metastasis in Luminal A type breast cancer patients is lower than that in Luminal type B breast cancer patients, and there are some differences in clinicopathological and ultrasonic characteristics, and The prognosis of luminal type A breast cancer is better than that of luminal type B breast cancer.

**Key words:** Breast cancer; Luminal type A; Luminal type B; Axillary lymph node; Metastasis; Prognosis

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## 前言

近年来,随着人们生活方式的不断改变,乳腺癌的发病率逐年增长<sup>[1,2]</sup>。乳腺癌是我国女性所有恶性肿瘤中发病率最高的一种恶性肿瘤疾病,且病死率较高,严重威胁我国女性生命健康安全<sup>[3]</sup>。相关研究报道表明<sup>[4]</sup>,组织学分类相同的乳腺癌患者预后亦可能存在一定的差异。随着分子生物学技术的广泛应用,乳腺癌分子分型逐渐成为临床广大医务人员研究的热点<sup>[5]</sup>。2011年的《St.Gallen 早期乳腺癌初始治疗国际专家共识》<sup>[6]</sup>中将乳腺癌分成管腔A型(Luminal A型)、管腔B型(Luminal B型)、人表皮生长因子受体-2(Human epidermal growth factor receptor-2, HER-2)过表达型以及基底细胞样型4种分子亚型,其中Luminal A型和Luminal B型同属激素受体阳性,但在临床治疗以及预后方面存在显著差异<sup>[7]</sup>。鉴于此,本研究通过对比Luminal A型和Luminal B型乳腺癌患者的腋窝淋巴结转移发生率及预后情况,旨在为乳腺癌患者的临床诊治提供参考依据,现作以下报道。

## 1 资料与方法

### 1.1 一般资料

回顾性分析我院从2011年5月~2014年12月收治的乳腺癌患者180例作为研究对象。年龄31~79岁,平均(48.32±11.73)岁;肿瘤大小1.4~5.0 cm,平均(2.33±0.45)cm;有家族史者5例,正处于绝经状态下患者93例;体质质量指数(Body mass index,BMI)18.4~28.1 kg/m<sup>2</sup>,平均(23.84±2.39)kg/m<sup>2</sup>;组织分级:I级59例,II级67例,III级54例;导管癌121例,非导管癌59例,包括粘液腺癌32例,小叶癌13例,髓样癌8例,化生性癌6例。纳入标准:(1)所有受试者均经病理组织活检确诊为乳腺癌;(2)均符合Luminal A型或Luminal B型乳腺癌相关诊断标准<sup>[8]</sup>;(3)入院前未接受相关抗肿瘤治疗者;(4)临床病历资料完整。排除标准:(1)其他分子类型乳腺癌患者;(2)合并

其他恶性肿瘤者;(3)意识障碍或伴有精神疾病者;(4)正参与其他研究者;(5)研究过程中因各种原因退出者或脱落病例。纳入对象均在知情同意书上签字,并获批于医院伦理委员会。

### 1.2 研究方法

(1)分组方式:以免疫组织化学法检测孕激素受体(Progesterone receptor, PR)、雌激素受体(Estrogen receptor, ER)、ki67以及HER-2等指标表达水平,将其按照临床病理类型的差异分成Luminal A型组84例与Luminal B型组96例(其中Luminal A型评价标准为ER阳性和/或PR阳性,且HER-2阴性;Luminal B型评价标准为ER阳性和/或PR阳性,且HER-2阳性)。(2)临床病理特征信息采集:以我院自制的患者临床病理特征调查表进行患者各项临床病理特征信息的统计、记录,具体内容包括年龄、肿瘤大小、家族史、绝经状态、BMI、组织分级以及病理分型等。(3)对所有受试者均进行为期5年的随访观察,统计复发转移率以及生存率。(4)超声检查:采用美国ALOKA-5-B彩色多普勒超声诊断仪进行超声检查,高频线阵探头,频率1~15MHz。检查前要求所有患者均取仰卧位,高举双手,充分暴露双侧乳腺和腋窝,将乳头作为中心,实施放射状的持续性扫查,发现病灶重点观察肿块位置、形态、边界、内部回声以及后方回声等特征。(5)采用Adler半定量法对肿块内的血流丰富程度进行分级<sup>[9]</sup>:无血流即为I级;少量血流即为II级;血流丰富即为III级。

### 1.3 统计学方法

数据的分析借助SPSS20.0软件完成,计数资料以[n(%)]表示,实施χ<sup>2</sup>检验。 $P<0.05$ 表示差异具有统计学意义。

## 2 结果

### 2.1 两组临床病理特征对比

Luminal A型组年龄>50岁、肿瘤大小≤2 cm、组织分级I级人数占比均高于Luminal B型组( $P<0.05$ ),两组家族史、绝经状态、BMI、病例分型对比无统计学差异( $P>0.05$ ),见表1。

表1 两组临床病理特征对比【例(%)】

Table 1 Comparison of clinicopathological features between the two groups[n(%)]

Clinicopathological features	Luminal type A group(n=84)	Luminal type B group(n=96)	χ <sup>2</sup>	P
Age(years)	≤ 50 40(47.62)	61(63.54)	4.612	0.032
	>50 44(52.38)	35(36.46)		
Tumor size(cm)	≤ 2 50(59.52)	37(38.54)	7.898	0.005
	>2 34(40.48)	59(61.46)		
Family history	Yes 2(2.38)	3(3.13)	0.092	0.762
	No 82(97.62)	93(96.87)		
Menopausal state	Yes 43(51.19)	50(52.08)	0.014	0.905
	No 41(48.81)	46(47.92)		
BMI(kg/m <sup>2</sup> )	≤ 24 45(53.57)	52(54.17)	0.006	0.936
	>25 39(46.43)	44(45.83)		
Tissue degree	I grade 43(51.19)	16(16.67)	24.234	0.000
	II~III grade 41(48.81)	80(83.33)		
Pathological type	Duct cancer 65(77.38)	76(79.17)	0.084	0.772
	Non-Duct cancer 19(22.62)	20(20.83)		

## 2.2 两组腋窝淋巴结转移情况对比

Luminal A 型组腋窝淋巴结转移发生率为 13.10%(11/84),

显著低于 Luminal B 型组的 39.58%(38/96)( $P<0.05$ ), 见表 2。

表 2 两组腋窝淋巴结转移情况对比

Table 2 Comparison of axillary lymph node metastasis between the two groups

Groups	n	Non-metastases	Metastases	Metastases rate(%)
Luminal type A group	84	73	11	13.10
Luminal type B group	96	58	38	39.58
$\chi^2$	-	-	-	15.866
P	-	-	-	0.000

## 2.3 两组患者 5 年复发转移率以及生存率对比

Luminal A 型组和 Luminal B 型组患者的 5 年复发转移率对比差异无统计学意义 ( $P>0.05$ ); Luminal A 型组 5 年生存率

为 86.90%(73/84), 高于 Luminal B 型组的 73.96%(71/96) ( $P<0.05$ ), 见表 3。

表 3 两组患者 5 年复发转移率以及生存率对比【例(%)】

Table 3 Comparison of the 5-year recurrence and metastasis rate and survival rate between the two groups[n(%)]

Groups	n	Recurrent metastatic rate	Survival rate
Luminal type A group	84	14(16.67)	73(86.90)
Luminal type B group	96	23(23.96)	71(73.96)
$\chi^2$	-	1.459	4.693
P	-	0.227	0.030

## 2.4 两组超声学特征对比

Luminal A 型组边界清晰、无钙化人数占比均高于 Luminal B 型组( $P<0.05$ ), 而 Alder 为 III 级人数占比低于 Luminal B 型组( $P<0.05$ ), 见表 4。

## 3 讨论

迄今为止, 关于乳腺癌的具体病因尚未彻底明确, 普遍认为可能和家族史、未哺乳和未生育、一侧已患乳腺癌、腺体致密、高脂饮食、乳腺增生以及卵巢内分泌紊乱等有关<sup>[10-12]</sup>。伴随着肿瘤临床个体化治疗的开展以及乳腺癌基因表达谱的深入研究, 不同乳腺癌亚型的临床特征以及对治疗的反应、预后具

表 4 两组超声学特征对比【例(%)】

Table 4 Comparison of the ultrasonic characteristics between the two groups[n(%)]

Ultrasonic characteristics		Luminal type A group(n=84)	Luminal type B group(n=96)	$\chi^2$	P
Shape	Rule	9(10.71)	12(12.50)	0.139	0.710
	Un-rule	75(89.29)	84(87.50)		
Boundary	Clear	24(28.57)	14(14.58)	5.263	0.022
	Vague	60(71.43)	82(85.42)		
Internal echo	Even	17(20.24)	21(21.88)	0.072	0.788
	Un-even	67(79.76)	75(78.12)		
Calcification	Yes	16(19.05)	38(39.58)	8.997	0.003
	No	68(80.95)	58(60.42)		
Alder	0	13(15.48)	15(15.63)	5.092	0.014
	I	33(39.29)	18(18.75)		
	III	31(36.90)	55(57.29)		
Rear Echo	IV	7(8.33)	8(8.33)	0.725	0.642
	No significant change	43(51.19)	47(48.96)		
	Strengthen	3(3.57)	5(5.21)		
	Collapse	38(45.24)	44(45.83)		

有较大的差异<sup>[13-15]</sup>。21世纪早期,美国临床肿瘤学会拟将ER、PR、HER-2免疫组化结果作为乳腺癌的一种新型分型指标,将以此分成Luminal A型、Luminal B型、HER-2过表达型以及基底细胞样型<sup>[16-18]</sup>。另有研究报道显示,乳腺癌患者的ki-67表达水平和内分泌治疗及预后密切相关,且可将ki-67作为一种有效鉴别诊断Luminal A型、Luminal B型乳腺癌的指标<sup>[19,20]</sup>。随着分子生物学研究技术的逐渐深入,通过检测肿瘤组织和肿瘤细胞内基因表达情况实现乳腺癌的分子分型,有利于解决肿瘤异质性问题,继而为临床乳腺癌个体化治疗方案的制定提供极其重要的指导作用<sup>[21-23]</sup>。

本研究结果发现,Luminal A型组年龄>50岁、肿瘤大小≤2cm、组织分级I级人数占比均高于Luminal B型组。白鸽等人的研究结果显示<sup>[24]</sup>,Luminal A型乳腺癌患者的年龄相较Luminal B型更高,而肿瘤相较Luminal B型更小,组织分级相比Luminal B型更低。两项研究相似,说明了Luminal B型乳腺癌患者的临床病理学特征相对较差。因此,在临床实际工作中应重点关注Luminal B型乳腺癌患者,此外,Luminal A型组腋窝淋巴结转移发生率为13.10%,显著低于Luminal B型组的39.58%,提示了Luminal B型乳腺癌患者相较于Luminal A型乳腺癌患者发生腋窝淋巴结转移的风险更高。分析原因,可能是乳腺癌患者的腋窝淋巴结转移发生和多种因素密切相关,包括年龄、肿瘤大小、组织学分级、疾病史、家族史以及生活行为因素等,即随着年龄的增长、肿瘤大小的降低、组织学分级的下降,乳腺癌患者的腋窝淋巴结转移风险越低<sup>[25-27]</sup>,而Luminal B型乳腺癌患者的年龄普遍低于Luminal A型乳腺癌患者,肿瘤大小以及组织学分级均明显高于Luminal A型乳腺癌患者,因此,相较于Luminal A型乳腺癌患者,Luminal B型乳腺癌患者具有更高的腋窝淋巴结转移风险,在临床工作中应密切关注Luminal B型乳腺癌患者腋窝淋巴结转移情况,并针对患者的具体病情制定相关治疗方案,以期达到改善患者预后的目的。本次研究还统计发现,32例粘液腺癌中Luminal A型乳腺粘液腺癌14例,Luminal B型乳腺粘液腺癌18例,Luminal A型乳腺粘液腺癌腋窝淋巴结转移2例,Luminal B型乳腺粘液腺癌腋窝淋巴结转移7例,组间差异有统计学意义( $P<0.05$ ),该结果虽未在本次研究结果中呈现,但在后续的报道中,可对乳腺癌分析做更细致的分型分析。另外,Luminal A型组和Luminal B型组患者的5年复发转移率对比差异无统计学意义,Luminal A型组5年生存率为86.90%,高于Luminal B型组的73.96%,这提示了Luminal B型乳腺癌患者的预后相较于Luminal A型乳腺癌患者更差。究其原因,可能和Luminal B型乳腺癌患者分化较差、淋巴结受累等相关。因此,针对Luminal A型乳腺癌患者可以内分泌治疗方案为主,而针对Luminal B型乳腺癌患者应以化疗联合内分泌治疗为主<sup>[28]</sup>。本研究结果还显示了Luminal A型组边界清晰、无钙化人数占比均高于Luminal B型组,而Alder为III级人数占比低于Luminal B型组,这再次证实了Luminal A型乳腺癌边界多清晰,且无钙化,血供相对不足,同时也说明了在临床工作中可能通过对乳腺癌患者进行超声检查,继而有助于鉴别诊断Luminal A型和Luminal B型乳腺癌<sup>[29,30]</sup>。

综上所述,Luminal A型乳腺癌患者的腋窝淋巴结转移发

生率低于Luminal B型乳腺癌患者,且预后明显更好,Luminal A型与Luminal B型在临床病理和超声学特征存在一定的差异。

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