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· 临床研究 ·

乳腺导管原位癌行前哨淋巴结活检指征的探讨*

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摘要 目的:分析乳腺导管原位癌的前哨淋巴结临床及病理特征,探讨乳腺导管原位癌患者实施前哨淋巴结活检的指征。**方法:**回顾性分析2002年10月到2010年11月期间诊断为乳腺导管原位癌并行前哨淋巴结活检的46例患者的前哨淋巴结状态及其与其他临床及病理特征的关系。**结果:**患者的年龄、肿瘤大小、检出SLN数、肿瘤分级、切缘状态、DCIS类型、是否伴随坏死均无显著统计学意义($P>0.05$)。可能与乳腺导管原位癌患者前哨淋巴结阳性的几个因素为:年龄41岁-69岁、肿瘤大小1.1 cm-5.0 cm、切缘状态未知、肿瘤坏死伴随或未知、肿瘤分级Ⅰ级以上或未知。**结论:**以下几个因素可能对预测DCIS患者可能出现SLN阳性提供帮助,临床在遇到出现这些因素的DCIS患者需慎重考虑其治疗策略,这些因素包括:年龄41岁-69岁、肿瘤大小1.1 cm-5.0 cm、切缘状态未知、肿瘤坏死伴随或未知、肿瘤分级Ⅰ级以上或未知。

关键词:乳腺癌;导管原位癌;前哨淋巴结活检;淋巴结转移

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Discussion of the Sentinel Lymph Node Biopsy for the Treatment of Ductal Carcinoma in Situ*

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ABSTRACT Objective: To analyze the characteristics of the ductal carcinoma in situ patients who were undergoing the sentinel lymph node biopsy and to discuss the indications that ductal carcinoma in situ patients should undergo sentinel lymph node biopsy. **Methods:** A retrospective analysis was performed about the status of sentinel lymph node and their clinical and pathological characteristics of the ductal carcinoma in situ patients who were undergoing the sentinel lymph node biopsy in our hospital from October 2002 to November 2010. **Results:** The results of multiple logistic regression analysis showed that there was no statistically significant difference about these factors, including age, tumor size, number of SLN excised, tumor grade, margin status, type of DCIS or accompanied with necrosis ($P>0.05$). However, there were still some factors that might be correlative to the node positive of DCIS patients, which are age between 41-69, size of tumor 1.1 cm-5.0 cm, unknown status of the margin, with necrosis or unknown, tumor grade II III or unknown. **Conclusions:** It is suggested that the following factors could help to predict the DCIS for patients who were treated with the positive SLN and we should make careful decision on the treatment for the patients at the age of 41 to 69, with tumor size of 1.1 cm to 5.0 cm, unknown status of the margin, with necrosis or unknown, tumor grade II III or unknown.

Key words: Breast cancer; Ductal carcinoma in situ; Sentinel lymph node biopsy; Nodal metastasis

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前言

腋窝淋巴结分期对乳腺癌患者治疗方式的选择及预后非常重要。目前,临床上对早期乳腺癌前哨淋巴结进行活检(Sentinel Lymph Node Biopsy, SLNB)来代替腋窝淋巴结清扫(Axillary Lymph Node Dissection, ALND)对腋窝淋巴结进行分

期已逐渐被广泛应用。乳腺导管原位癌(Ductal Carcinoma in Situ, DCIS),又称导管内癌(Intraductal Carcinoma),是指癌细胞未突破导管壁基底膜。理论上,此类型乳腺癌不向周围组织浸润,也不发生淋巴结转移,因此不需要施行前哨淋巴结活检。术后最终病理证实为单纯DCIS的病例没有一例发生前哨淋巴结转移,而术前诊断为导管原位癌而术后最终病理诊断为浸

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润性导管癌的病例中,有5.4%的病例出现前哨淋巴结转移^[1]。即使出现SLN微转移或转移也不一定意味着预后差^[2]。随着乳腺癌筛查技术的提高和普及,越来越多的新发导管原位癌(占10%-20%)通过此方法被检出^[3,4]。而乳腺导管原位癌是否需行前哨淋巴结活检,有无可靠的指征来为每一例导管原位癌患者制定最佳的治疗方案,亟需进一步明确。回顾性分析我院2002年10月到2010年11月期间诊断为乳腺导管原位癌并行前哨淋巴结活检的46例患者的前哨淋巴结状态,探讨其与临床及病理特征的关系。现将结果汇报如下:

1 资料与方法

1.1 一般资料

所有患者均为女性,年龄分布在28-71岁,平均年龄为45岁,其中小于60岁者41例(占总数的89.1%)。病程最短为3

天,最长为10年,中位病程40天。术前和(或)术后诊断为单纯性导管原位癌或导管原位癌伴微浸润或浸润、小叶原位癌、page's病,46例患者均在术前或术中施行前哨淋巴结活检。按照是否出现SLN阳性,分为SLN阳性组(3例)和SLN阴性组(43)例。

1.2 手术方式

18例行保乳手术,18例行乳房全切,8例行改良根治术,1例行保留乳头乳晕皮肤腺体全切,1例行保留乳头皮肤的乳房全切后即刻再造。

1.3 肿瘤大小的确定

并非每例患者都常规行B超+磁共振+钼靶照相,且针穿活检诊断为DCIS的患者不常规推荐术前腋窝超声检查^[5]。为了可对比性,采集了临床查体所触及肿瘤大小数据。

1.4 病理资料的获取

表1 不同临床病理因素与前哨淋巴结阳性的关系

Table 1 Relationship of positive SLN with different clinical and pathological factors

Clinical & Pathological Factors		Caese	Percentages(%)	SLN(cases)			
				Cases of SLN excised	Cases of positive SLN	Positive SLN in each group (%)	Positive of total excised SNL(%)
Age	≤40	14	30.4	33	0	0	0
	41-69	31	67.4	73	3	4.1	2.8
	≤70	1	2.2	1	0	0	0
	≤1	9	19.6	19	0	0	0
Tumor size	1.1-2.0	17	37.0	43	1	2.3	0.9
	2.1-5.0	17	37.0	39	2	5.1	1.9
	>5	3	6.5	6	0	0	0
	1	11	23.9	11	1	9.1	0.9
Excised SLN	2	20	43.5	40	1	2.5	0.9
	≥3	15	32.6	56	1	1.8	0.9
	I	4	8.7	6	0	0.0	0
	II	17	37.0	43	1	2.3	0.9
Tumor grade	III	2	4.3	3	1	33.3	0.9
	Unknown	23	50.0	55	1	1.8	0.9
	Positive	1	2.2	2	0	0	0
	Negative	13	28.3	34	0	0	0
Margin status	Hyperplasia	1	2.2	1	0	0	0
	Atypical	2	4.3	3	0	0	0
	Hyperplasia	29	63.0	67	3	4.5	2.8
	Unknown	0	71.7	0	0	-	-
Comedo type	+	6	37.0	19	1	5.3	0.9
	-	40	28.3	88	2	2.3	1.9
	Unknown	4	8.7	10	2	20.0	1.9
	+	2	4.3	3	0	0	0
With necrosis	-	2	4.3	3	0	0	0
	Unknown	40	87.0	94	1	1.1	0.9

临床病历资料记载的病理报告信息不完整的病例,重新查阅病理科原始资料,与病理科医师一起讨论确定肿瘤分级、是否伴随坏死、DCIS 类型、冰冻病理检查切缘情况等病理数据。

1.5 统计学分析

应用 SPSS 19.0 统计软件进行分析,采用多重 logistic 逐步回归模型来鉴别导致 SLN 阳性的预测因素。以 $P < 0.05$ 为差异具有统计学意义。

2 结果

2.1 统计资料及统计学处理结果

本组共搜集了 46 例患者,其临床及病理特征见表 1。多重 logistic 回归分析结果显示,年龄、肿瘤大小、检出 SLN 数、肿瘤分级、切缘状态、DCIS 类型、是否伴随坏死均无显著统计学意义(P 值均 > 0.05)。

2.2 多重 logistic 逐步回归模型未提示有显著临床意义的因素的原因

我们的研究数据在多重 logistic 回归分析的结果中未发现与 SLN 阳性有关的显著统计学意义的指标,这与一些因素的结果为“未知”且其病例数占总病历数比例较大等有关,这与回顾性分析临床资料的缺陷有关,另外与 SLN 阳性和阴性两组病例数相差较大也可能有关。

2.3 可能对临床提供预测的预测指标

所有 SLN 阳性都出现在 41 岁 -69 岁组、肿瘤大小 1.1 cm-5.0 cm 组、切缘状态未知组、肿瘤坏死伴随或未知组、肿瘤分级 I 级以上未知组。SLN 检查数与 SLN 是否阳性无关。

3 讨论

目前,大家普遍认为癌细胞未突破导管壁基底膜,理论上此类型乳腺癌不向周围组织浸润,也不发生淋巴结转移,因此不需要施行前哨淋巴结活检。但是仍有 DCIS 患者 SLN 阳性的病例出现。如果可以找到一些高危因素可以进行预测并制定出导管原位癌患者实施前哨淋巴结活检的标准,则患者可能在避免二次手术(SLNB 及随后可能的腋窝淋巴结清扫)、避免手术麻醉、术后疼痛、缓解心理压力及减少医疗费用等各个方面获益。目前达成共识的有:乳房全切及即时重建的患者在术中行 SLNB^[6];在术前应用对比增强 B 超引导下前哨淋巴结穿刺活检,如结果为阴性则在术中行常规 SLNB^[7]。Tomohiro Miyake^[1]认为出现可触摸到的肿块以及 MRI 提示 ≥ 2 cm 是导管原位癌可能同时隐匿有浸润性导管癌的高危因素。其他一些研究报道^[8-11]的高危因素为:由针吸穿刺诊断为 DCIS,穿刺时发现广泛钙化,肿瘤大小,高分级,切缘距离,伴随小叶癌化,激素受体状态,MR 的 DCE 和 DW 影像特征,BRCA 基因检测结果等。切缘距离争议较大,一些文献认为即使切缘太近或者切缘阳性,胸壁转移发生率很低,甚至无需术后放疗(PMRT)^[12,15]。

一个合理的治疗方式的制定,应该包括治疗失败后的补救措施,以期使患者得到最大的获益,SLN 阳性而未行腋窝淋巴结清扫的患者,无论术前是否进行过放射治疗,单独全乳房放疗可以提供足够的局部控制^[13,14]。继保乳术后放疗可明显降低复发率,之后仍可应用三苯氧胺以显著降低 ER 阳性患者继发性乳腺癌发生。这些研究都有利于我们大胆的探索 DCIS 患者

行 SLNB 的指征^[16-18]。

在我们的研究中,分析每个单独的因素可以发现,所有 SLN 阳性都出现在 41 岁 -69 岁组、肿瘤大小 1.1 cm-5.0 cm 组、切缘状态未知组、肿瘤坏死伴随或未知组、肿瘤分级 I 级以上未知组,这仍可以为我们提供一些线索。

41 岁 -69 岁组患者受雌激素作用时间长,身体代谢相对活跃,可能是 SLN 阳性全部出现在此组的主要原因。肿瘤小(≤ 1 cm)或太大(> 5 cm)则其恶性程度相对较低,这一结果与 Shelley H 等的研究结果^[19]一致,其研究显示高分级肿瘤越大预后越好。切缘状态未知,则有可能藏匿切除不完全而残留浸润性癌或其他类型癌,而导致 SLN 阳性全部集中在此组。肿瘤分级高级肿瘤伴随坏死,均提示肿瘤的恶性生物学行为较明显^[20]。我们的研究结果显示,以下几个因素可能对预测 DCIS 患者可能出现 SLN 阳性提供帮助,临床在遇到出现这些因素的 DCIS 患者需慎重考虑其治疗方式及策略,这些因素包括:年龄 41 岁 -69 岁、肿瘤大小 1.1 cm-5.0 cm、切缘状态未知、肿瘤坏死伴随或未知、肿瘤分级 I 级以上未知。

综上所述,随着乳腺癌筛查的发展,越来越多的早期乳腺癌将被发现,导管原位癌的在乳腺恶性肿瘤比例也逐步增加,进一步明确并制定导管原位癌行前哨淋巴结活检的标准将使更多的导管原位癌患者获益,而这有赖于大样本量的、多中心的、前瞻性的临床研究所提供的循证医学证据。

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