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乳腺癌患者的超声征象表现与组织学特征的关系研究*

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摘要 目的:研究乳腺癌患者的超声征象表现与组织学特征的关系。**方法:**收集自2012年5月-2016年5月在我院接受诊治的240例乳腺癌患者作为研究对象,所有患者手术前接受超声检查,分析超声征象与病理组织学分型、分级以及雌激素受体(ER)、孕激素受体(PR)表达之间的关系。**结果:**240例乳腺癌患者中,有57例(23.75%)呈规则形态,183例(76.25%)呈不规则形态;171例(71.25%)肿块边界有毛刺,69例(28.75%)肿块无毛刺;210例(87.50%)肿块呈现后方回声无衰减或增强,30例(12.50%)肿块呈现后方回声衰减;118例(49.17%)出现微小钙化,122例(50.83%)没有出现微小钙化。在不同病理学分型中,不规则形态、肿块边界毛刺发生率具有明显差异($P<0.05$),不规则形态发生率由高到低的顺序为:浸润性小叶癌、浸润性导管癌、导管内癌、特殊类型癌,浸润性导管癌和浸润性小叶癌边界毛刺发生率显著高于导管内癌和特殊类型癌($P<0.05$),而在不同病理组织学分型、病理学分级、ER表达、PR表达中,后方回声衰减、微小钙化发生率比较无明显差异($P>0.05$)。**结论:**乳腺癌超声征象表现与病理组织学特征密切相关,超声诊断对于病理组织学类型具有一定的预测作用。

关键词:乳腺癌;超声征象;病理组织学;分级

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Study on the Relationship between Ultrasonographic Signs and Histological Characteristics of Breast Cancer Patients*

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ABSTRACT Objective: To study the relationship between ultrasonographic signs and histological characteristics of breast cancer patients. **Methods:** 240 patients with breast cancer treated in our hospital from May 2012 to May 2016 were enrolled as research object. All patients received ultrasonic examination before operation. The relationship between the ultrasonographic signs and histopathological classification, grading, the expression of estrogen receptor (ER), progesterone receptor (PR) were analyzed. **Results:** In 240 cases of breast cancer patients, there were 57 cases (23.75%) showed regular morphology and 183 cases (76.25%) showed irregular morphology. 171 cases (71.25%) had burr in tumor boundary, 69 cases (28.75%) had not burr in tumor boundary. 210 cases (87.50%) presented had no attenuation or enhancement in posteroecho and 30 cases (12.50%) had attenuation in posteroecho. 118 cases (49.17%) had slight calcification and 122 cases (50.83%) had no calcification. The incidence rate of irregular morphology and tumor boundary burr had obvious differences in different pathological types ($P<0.05$). The incidence rate of irregular morphology from high to low was infiltrating lobular carcinoma, infiltrating ductal carcinoma, intraductal carcinoma and special type carcinoma. The incidence rate of boundary burr in infiltrating ductal carcinoma and infiltrating lobular carcinoma was significantly higher than that in intraductal carcinoma and special type carcinoma ($P<0.05$). There was no significant difference in the incidence rate of posterior echo attenuation and microcalcification between different histopathological classification, pathological grading, ER expression and PR expression ($P>0.05$). **Conclusion:** The ultrasonographic signs of breast cancer are closely related to the histopathological characteristics, and the ultrasound diagnosis has certain predictive effect on the histopathological types.

Key words: Breast cancer; Ultrasonographic signs; Histopathology; Grading

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前言

乳腺癌是一种女性常见的恶性肿瘤,近年来乳腺癌的发病率逐年上升,对女性的生命健康构成巨大的威胁^[1,2]。在乳腺癌早期患者无明显的临床体征,从而较难被患者察觉,导致多数

患者确诊时已是晚期,因此在乳腺癌早期进行准确有效的诊断成为临床研究的热点,早诊断、早治疗对降低患者的死亡率、提高患者的五年生存率具有十分重要的意义^[3,4]。目前应用于乳腺癌早期辅助诊断的方法很多,如钼靶X线、超声检查、核磁共振(Magnetic resonance imaging, MRI)增强,最后通过穿刺活检

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的方法得到确诊。钼靶 X 线对乳腺癌的灵敏度及特异性较彩超明显提高,但是该项检查操作复杂、读片误差较大、对医生的要求较高,从而限制了它的使用^[5,6]。有研究表明,MRI 对乳腺癌的诊断价值高于钼靶 X 线,但是该项检查价格昂贵并且存在辐射,对患者造成不良影响,因此在临床实际应用中受到限制^[7,8]。超声检查的优点在于价格低廉、无辐射等副作用,能够清晰的观察乳腺癌的早期病变,在临床得到广泛应用^[9]。本研究主要探讨乳腺癌患者超声征象与组织学特征之间的关系,为提高超声诊断乳腺癌的价值提供相关的理论依据。

1 资料与方法

1.1 一般资料

选取 2012 年 5 月-2016 年 5 月在我院接受诊治的乳腺癌患者 240 例,均为女性,年龄 27-75 岁,平均(55.1±6.1)岁,纳入标准:①所有病例均经临床和手术病理证实;②所有患者临床资料和超声影像学资料完整。排除标准:①合并其他脏器或组织肿瘤者;②妊娠期或哺乳期患者;③既往有乳腺手术病史者。所有患者或家属知情同意并签署知情同意书,本研究经医院伦理委员会审核通过。

1.2 仪器与超声检查

本研究中所使用的仪器为 PHILIPS IU 22 超声仪 L12-5 探头,探头频率为 5.0-12.0 MHz。患者仰卧位,充分暴露乳房,根据每位患者的实际情况调整焦距部位、深度,使图像达到最佳状态。重点观察肿块形态是否规则、边界是否有毛刺、后方回声是否衰减、是否出现微小钙化等征象。采集典型图像,存盘备用。由一位主治以上超声医师分析评价图像,记录结果,乳腺癌的超声征象定义参考 Stavros AT 等^[10]的标准。

1.3 乳腺癌病理类型及组织学分级

乳腺癌的病理学分型严格按照诊断标准进行^[11],非浸润性癌:小叶原位癌以及导管内癌;浸润性癌:浸润性小叶癌、浸润性导管癌以及特殊类型癌。乳腺癌的组织学分级参照 Bloom Richardson 分级标准进行^[12],即 I 级:腺管量>75%,肿瘤细胞核小而规则,在细胞生长活跃区,细胞核分裂每 10HPF 为 0-5 个;II 级:腺管量为 10%-75%,肿瘤细胞核大而规则,细胞核分

裂每 10HPF 为 6-10 个;III 级:腺管量<10%,肿瘤细胞核大而不规则,核仁明显,细胞核分裂每 10HPF≥11 个。

1.4 雌激素受体 (estrogen receptor,ER) 和孕激素受体 (progesterone receptor,PR)测定

所有患者的病理标本均来源于病理检查时所取标本留样,处理方法如下:用福尔马林固定癌组织,切片行石蜡包埋;切片后遵循免疫组化试剂盒(北京中杉金桥生物公司)说明书进行相应的操作,再进行染色。一抗为鼠抗人 ER、PR 抗体、二抗及染色试剂购自 Santa 公司。每张切片于 10×40 倍镜下随机取 5 个视野进行观察,分别计数染色的阳性细胞占全部癌细胞的百分比。对结果进行判读,主要根据以下两方面:①染色的阳性细胞所占百分比:<1%则记为 0 分,1%~10%则记为 1 分,10%~30%则记为 2 分,30%~60%则记为 3 分,>60%则记为 4 分;②阳性细胞的染色强弱:无染色为 0 分,淡黄色为 1 分,棕黄色为 2 分,棕褐色为 3 分。最终结果判定:两评分的乘积在 0-2 分范围内为阴性,≥3 分为阳性。

1.5 统计学处理

数据采用 SPSS20.0 软件进行统计分析,计数资料以率(%)表示,两组数据比较采用 χ^2 检验, $P<0.05$ 则表明差异具有统计学意义。

2 结果

2.1 乳腺癌肿块形态与临床病理特征的关系

对本研究 240 例乳腺癌患者进行病理组织学分型,具体为:导管内癌 22 例、浸润性导管癌 187 例、浸润性小叶癌 12 例、特殊类型癌 19 例。病理组织学分级具体为:I 级 146 例,II 级 67 例,III 级 27 例。ER 表达阳性 175 例,阴性 65 例。PR 表达阳性 209 例,阴性 31 例。240 例乳腺癌患者中,有 57 例(23.75%)呈规则形态,183 例(76.25%)呈不规则形态。在不同病理学分型中,不规则形态发生率具有统计学差异($P<0.05$),不规则形态发生率由高到低的顺序为:浸润性小叶癌、浸润性导管癌、导管内癌、特殊类型癌。在不同病理学分级、ER 表达以及 PR 表达中,不规则形态发生率比较无统计学差异($P>0.05$),见表 1。

表 1 乳腺癌肿块形态与临床病理特征的相关性[n(%)]

Table 1 Correlation between tumor morphology and clinicopathological features of breast cancer[n(%)]

Clinicopathological features		Regular morphology (n=57)	Irregular morphology(n=183)	χ^2	P
Histopathological classification	Intraductal carcinoma	8(36.36)	14(63.64)	4.567	0.046
	Infiltrating ductal carcinoma	40(21.39)	147(78.61)		
	Infiltrating lobular carcinoma	1(8.33)	11(91.67)		
	Special type carcinoma	8(42.11)	11(57.89)		
Histopathological grading	Grade I	32(21.92)	114(78.08)	1.465	0.128
	Grade II	20(29.85)	47(70.15)		
	Grade III	5(18.52)	22(81.48)		
ER expression	Positive	45(25.71)	130(74.29)	0.664	0.345
	Negative	12(18.46)	53(81.54)		
PR expression	Positive	48(22.97)	161(77.03)	0.542	0.664
	Negative	9(29.03)	22(70.97)		

2.2 乳腺癌肿块边界毛刺与临床病理特征的关系

240 例乳腺癌患者中,一共有 171 例(71.25%)肿块边界有毛刺,69 例(28.75%)肿块无毛刺,在不同病理学分型中,肿块边界毛刺发生率具有统计学差异($P<0.05$),浸润性导管癌和浸

润性小叶癌边界毛刺发生率显著高于导管内癌和特殊类型癌($P<0.05$)。在不同病理学分级、ER 以及 PR 表达中,肿块边界毛刺发生率比较无统计学差异($P>0.05$),见表 2。

表 2 乳腺癌肿块边界毛刺与临床病理特征的相关性[n(%)]

Table 2 Correlation between boundary burr and clinicopathological features of breast cancer[n(%)]

Clinicopathological features		Boundary burr(n=171)	No boundary burr(n=69)	χ^2	P
Histopathological classification	Intraductal carcinoma	8(36.36)	14(63.64)	3.982	0.005
	Infiltrating ductal carcinoma	147(78.61) [#]	40(21.39)		
	Infiltrating lobular carcinoma	9(75.00) [#]	3(25.00)		
	Special type carcinoma	7(36.84)	12(63.16)		
Histopathological grading	Grade I	102(69.86)	44(30.14)	0.572	0.091
	Grade II	53(79.10)	14(20.90)		
	Grade III	16(59.26)	11(40.74)		
ER expression	Positive	128(73.14)	47(26.86)	0.976	0.543
	Negative	43(66.15)	22(33.85)		
PR expression	Positive	147(70.33)	62(29.67)	1.467	0.145
	Negative	24(77.42)	7(22.58)		

Note: compared with intraductal carcinoma, [#] $P<0.05$; compared with the special type of cancer, ⁺ $P<0.05$.

2.3 乳腺癌肿块后方回声衰减与临床病理特征的关系

240 例乳腺癌患者中,一共有 210 例(87.50%)肿块呈现后方回声无衰减或增强,30 例(12.50%)后方回声衰减,在不同病

理学分型、病理学分级、ER 表达以及 PR 表达中,后方回声衰减发生率比较无统计学差异($P>0.05$),见表 3。

表 3 乳腺癌肿块后方回声衰减与临床病理特征的相关性[n(%)]

Table 3 Correlation between posterior echo attenuation and clinicopathological features of breast cancer mass[n(%)]

Clinicopathological features		Posterior echo had no attenuation or enhancement(n=210)	Posterior echo attenuation (n=30)	χ^2	P
Histopathological classification	Intraductal carcinoma	18(81.82)	4(18.18)	1.264	0.375
	Infiltrating ductal carcinoma	164(87.70)	23(12.30)		
	Infiltrating lobular carcinoma	11(91.67)	1(8.33)		
	Special type carcinoma	17(89.47)	2(10.53)		
Histopathological grading	Grade I	133(91.09)	13(8.91)	1.173	0.412
	Grade II	55(82.09)	12(17.91)		
	Grade III	22(81.48)	5(18.52)		
ER expression	Positive	157(89.71)	18(10.29)	0.162	0.812
	Negative	53(81.54)	12(18.46)		
PR expression	Positive	184(88.04)	25(11.96)	0.653	0.642
	Negative	26(83.87)	5(16.13)		

2.4 乳腺癌肿块微小钙化与临床病理特征的关系

240 例乳腺癌患者中,一共有 118 例(49.17%)出现微小钙化,122 例(50.83%)没有出现微小钙化。在不同病理学分型、病理学分级、ER 表达以及 PR 表达中,微小钙化发生率比较无统计学差异($P>0.05$),见表 4。

3 讨论

乳腺癌是指乳腺上皮组织发生的恶性病变,其对患者的生命健康和生活质量造成巨大的影响^[13]。据统计,全球每年约有 138.4 万人患上乳腺癌,约 45.8 万人因乳腺癌去世,且乳腺癌

表 4 乳腺癌肿块微小钙化与临床病理特征的相关性[n(%)]

Table 4 Correlation between microcalcification and clinicopathological features of breast cancer[n(%)]

Clinicopathological features		Microcalcification(n=118)	No microcalcification(n=122)	χ^2	P
Histopathological classification	Intraductal carcinoma	10(45.45)	12(54.55)	0.215	0.712
	Infiltrating ductal carcinoma	93(49.73)	94(50.27)		
	Infiltrating lobular carcinoma	6(50.00)	6(50.00)		
	Special type carcinoma	9(47.37)	10(52.63)		
Histopathological grading	Grade I	74(50.68)	72(49.32)	0.162	0.812
	Grade II	30(44.78)	37(55.22)		
	Grade III	14(51.85)	13(48.15)		
ER expression	Positive	89(50.86)	86(49.14)	0.245	0.654
	Negative	29(44.62)	36(55.38)		
PR expression	Positive	102(48.80)	107(51.20)	1.467	0.145
	Negative	16(51.61)	15(48.39)		

患者有年轻化的趋势, 因此乳腺癌的早期诊断显得尤为重要^[14]。超声检查是临床常用的检测乳腺癌的辅助手段, 它拥有经济、快捷、无辐射、准确性高、易被患者接受等优点, 乳腺癌的超声征象主要有: 形态不规则、后方回声衰减、边界毛刺、内部微小钙化, 但是临床发现部分患者超声影像学特征不典型, 会给临床医生的诊断带来困扰^[15, 16]。乳腺癌的病理组织学分型通常包括非浸润性癌和浸润性癌两大类, 前者包括导管内癌和小叶原位癌, 后者包括浸润性导管癌、浸润性小叶癌和特殊类型癌, 其中浸润性导管癌、浸润性小叶癌最为常见, 乳腺癌的病理组织学分型不同, 病情的发展、治疗及预后也不一样^[17]。ER 与 PR 是乳腺癌内分泌治疗及其预后的重要分子生物学指标, 本研究分析患者超声征象与病理组织学分型、分级以及 ER、PR 的关系, 为临床医生诊断乳腺癌提供参考依据^[18]。

在本研究 240 例乳腺癌患者中, 有 57 例(23.75%)呈规则形态, 183 例(76.25%)呈不规则形态。这表明形态不规则是乳腺癌超声检查的可靠指标。在不同病理学分型中, 不规则形态发生率具有明显差异($P < 0.05$), 不规则形态发生率由高到低的顺序为: 浸润性小叶癌、浸润性导管癌、导管内癌、特殊类型癌, 这表明形态不规则有可能是由于肿瘤病变沿乳腺导管浸润所致, 浸润性癌患者肿块常常表现为浸润性生长、间质纤维化组织明显增生, 所以超声检查多表现为不规则形态^[19, 20]。在不同病理学分级、ER 表达情况、PR 表达情况中, 不规则形态发生率比较无明显差异($P > 0.05$)。这表明肿瘤形态很难判断乳腺癌的分级以及 ER、PR 的表达情况。肿块边界毛刺、后方回声衰减以及微小钙化也是超声征象的重要指标^[21], 本研究结果显示, 240 例乳腺癌患者中, 有 171 例(71.25%)肿块边界有毛刺, 69 例(28.75%)肿块无毛刺; 有 210 例(87.50%)肿块呈现后方回声无衰减或增强, 30 例(12.50%)后方回声衰减; 有 118 例(49.17%)出现微小钙化, 122 例(50.83%)没有出现微小钙化。更进一步的研究显示, 在不同病理学分型中, 肿块边界毛刺发生率具有

明显差异($P < 0.05$), 浸润性导管癌和浸润性小叶癌边界毛刺发生率显著高于导管内癌和特殊类型癌边界毛刺的发生率, 边界毛刺征象所对应的病理学癌变为乳腺癌实质向周围组织浸润, 并伴有不同程度的间质反应^[22, 23], 本研究与浸润性癌的生物特性相吻合, 在不同病理学分级、ER 表达情况、PR 表达情况中, 肿块边界毛刺发生率比较无明显差异($P > 0.05$)。Ohta T 等^[24]和 Lai HW 等^[25]的研究证明, 后方回声衰减对于鉴别诊断浸润性小叶癌具有重要的临床意义, 但是本研究显示在不同病理学分型、病理学分级、ER 表达情况、PR 表达情况中, 微小钙化发生率、后方回声衰减发生率比较无明显差异($P > 0.05$), 这可能与本研究的样本量较少有关。

综上所述, 乳腺癌超声征象表现与病理组织学特征密切相关, 超声诊断对于病理组织学类型具有一定的预测作用。

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