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超声造影联合超声弹性成像组织弥散定量分析在乳腺癌诊断中的应用*

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摘要 目的:探讨超声造影联合超声弹性成像组织弥散定量分析在乳腺癌诊断中的应用价值。**方法:**2019年1月至2020年5月选择在本院诊治的乳腺肿瘤患者148例,所有患者都给予超声造影联合超声弹性成像组织弥散定量分析,记录影像学特征。**结果:**在148例患者中,病理诊断为乳腺癌32例(恶性组),良性乳腺肿瘤116例(良性组)。良性组与恶性组的超声病灶形状、边缘、回声、微钙化等特征对比差异有统计学意义($P<0.05$)。恶性组的超声造影增强模式、强度与良性组对比差异都有统计学意义($P<0.05$)。恶性组的造影灌注参数曲线下面积(Area under the curve, AUC)、峰值强度(Peak intensity, PI)、上升支斜率(Wash in slope, WIS)值都高于良性组,达峰时间(Time To Peak, TTP)值低于良性组,对比差异都有统计学意义($P<0.05$)。恶性组的组织弥散定量参数蓝色区域面积百分比(area ratio, %AREA)低于良性组,标准差(standard deviation, SD)、应变均值(mean, MEAN)值高于良性组,对比差异都有统计学意义($P<0.05$)。**结论:**超声造影联合超声弹性成像组织弥散定量分析在乳腺癌诊断中的应用作为一种经济快捷、实时无创、重复性好的检查方法,能够定量评估乳腺癌的影像学特征,可为乳腺癌的临床治疗提供更多有价值的信息。

关键词:超声造影;超声弹性成像组织弥散定量;乳腺癌;峰值强度;达峰时间

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Application of Ultrasound Contrast Combined with Ultrasound Elastography Quantitative Analysis of Tissue Diffusion in the Diagnosis of Breast Cancer*

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ABSTRACT Objective: To explore the application values of ultrasound contrast combined with ultrasound elastography quantitative analysis of tissue diffusion in the diagnosis of breast cancer. **Methods:** From January 2019 to May 2020, 148 cases of breast tumor patients were selected for diagnosis and treatment in our hospital. All patients were given ultrasound contrast combined with ultrasound elastography for quantitative analysis of tissue diffusion, and the imaging characteristics were recorded. **Results:** There were 32 cases were diagnosed as breast cancer by pathology (malignant group) and 116 cases were benign breast tumors (benign group) in the 148 cases. The benign group and malignant group compared were statistically significant differences in ultrasound lesion shape, margin, echo, microcalcification and other characteristics ($P<0.05$). The contrast enhancement mode and intensity of ultrasound contrast in the malignant group were significantly different from those in the benign group ($P<0.05$). The area under the curve (AUC), Peak intensity (PI), and wereh in slope (WIS) values of the malignant group were higher than those of the benign group, and the Time To Peak(TTP) values were lower than the benign group, and the contrast difference were statistically significant ($P<0.05$). The quantitative parameter of tissue diffusion in the malignant group were lower than the benign group in the blue area area ratio (% AREA), and the standard deviation (SD) and mean (MEAN) values were higher than the benign group($P<0.05$). **Conclusion:** The application of ultrasound contrast combined with ultrasonic elastography quantitative analysis of tissue dispersion in the diagnosis of breast cancer is an economical, fast, non-invasive, and reproducible examination method that can quantitatively assess the imaging characteristics of breast cancer clinical treatment provides more valuable information.

Key words: Ultrasound contrast; Quantitative tissue diffusion by ultrasound elastography; Breast cancer; Peak intensity; Peak time

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前言

乳腺癌是妇女的常见病,已成为发生率和死亡率增长最快的恶性肿瘤之一^[1]。尽管当前医疗诊疗技术不断地得到提高,但乳腺癌的总体预后并未得到显著改善,主要在于乳腺肿瘤的复发和转移。乳腺癌的早期发现、早期诊治是改善乳腺癌预后的关键,影像学诊断在乳腺肿瘤的发现和诊断中占有重要作用^[2,3]。超声具有无辐射、无创、实时等特点,特别是随着超声成像检查技术的日趋成熟,乳腺超声影像诊断从形态学诊断已经向功能学诊断方向发展,可以从形态学和血液动力学方面进行综合分析,从而提高乳腺癌的诊断敏感性与特异性^[4,5]。超声造影(contrast-enhanced ultrasound, CEUS)是一种能实时动态显示脏器微循环灌注的影像学技术,其造影剂微泡相当于红细胞大小,是一种纯血池造影剂,不会透过血管壁^[6,7]。并且超声造影可绘制出时间-强度(Intensity curve time, TIC)曲线,能量化增强数据,从而提高恶性肿瘤的检出^[8,9]。超声弹性成像组织弥散定量分析是当前研究的新技术,其是利用患者自身心血管搏动成像,克服了人为操作因素的影响,扩大了感兴趣区域的选择范围,提高了信号采集的敏感性,使得检测结果更加全面、准确^[10-12]。本文具体探讨了超声造影联合超声弹性成像组织弥散定量分析在乳腺癌诊断中的应用价值,以促进乳腺癌的早期检测。现总结报道如下。

1 资料与方法

1.1 研究对象

2019年1月至2020年5月选择在本院诊治的乳腺肿瘤患者148例,纳入标准:首次就诊并且接受完整治疗;女性单侧乳腺肿瘤;年龄30~70岁;检查前签署超声造影检查同意书,并告知患者相关风险;所有病理档案资料、个人资料与超声资料完整;超前检查前未行任何放、化疗等影响病灶发展的相关治疗;研究得到医院伦理委员会的批准。排除标准:男性乳腺肿瘤;双侧乳腺肿瘤;超声前接受过其他治疗者;妊娠与哺乳期妇女;因图像丢失或不完整者;伴随其他恶性肿瘤患者。

1.2 超声方法

采用GE Logic E9型超声诊断仪,配有ML6-15高频线阵探头,支持造影与弹性成像,造影剂选择Bracco公司的声诺维,超声机械指数为0.08。患者取平卧位,平静呼吸,将双臂上举放置于头两侧,充分显露乳腺,对乳腺进行全面扫查,对乳腺肿瘤的性质特征进行仔细观察。定位肿瘤部位,保持探头不变,经肘静脉推注配置好的SonoVue混悬液4.8 mL,然后注入生理盐水5.0 mL,记录造影特征并进行存储图像。然后启动弹性成像模式。取样框大小调整为2.5 cm×2.5 cm置于肿瘤部位,启

动数据处理系统,框定感兴趣区进行组织弥散定量分析。

1.3 观察指标

(1)记录所有患者的年龄、体重指数、病灶直径、病理特征,记录乳腺癌患者的临床分期、淋巴结转移、组织学分化情况。(2)记录所有患者的常规超声特征,包括病灶的形状、边缘、回声、微钙化等情况。(3)记录所有患者的超声造影增强模式与强度情况,增强强度分为高增强、低增强、等增强等;增强模式分为快进快出型、快进慢出型、其他型等。(4)选择病灶部位的感兴趣区(region of interest, ROI),记录造影的灌注参数,包括达峰时间(Time To Peak, TTP)、曲线下面积(Area under the curve, AUC)、峰值强度(Peak intensity, PI)、上升支斜率(Wash in slope, WIS)等指标。(5)记录所有患者的弹性参数,主要为蓝色区域面积百分比(area ratio, %AREA)、标准差(standard deviation, SD)、应变均值(mean, MEAN)等。

1.4 统计方法

使用SPSS 21.00统计学软件进行分析,计量数据以均数±标准差表示,计数数据以百分比表示,两两对比采用t检验与卡方 χ^2 检验,检验水准为 $\alpha=0.05$ 。

2 结果

2.1 病理结果

在148例患者中,病理诊断为乳腺癌32例(恶性组,浸润性小叶癌18例,髓样癌6例,小叶癌8例),良性乳腺肿瘤116例(良性组,乳腺纤维腺瘤67例,导管内乳头状瘤36例,乳腺囊肿13例)。

恶性组中年龄最小31岁,最大69岁,平均年龄 47.92 ± 4.11 岁;平均体重指数 22.48 ± 1.28 kg/m²;平均病灶直径 3.56 ± 0.11 cm;发病位置:左侧17例,右侧15例;临床分期:I期16例,II期10例,III期6例;淋巴结转移17例;组织学分化:高分化15例,中分化10例,低分化7例。

良性组中年龄最小28岁,最大70岁,平均年龄 48.02 ± 3.87 岁;平均体重指数 22.31 ± 1.11 kg/m²;发病位置:左侧59例,右侧57例。两组的年龄、体重指数、发病位置等对比差异无统计学意义($P>0.05$)。

2.2 常规超声特征对比

良性组与恶性组的超声病灶形状、边缘、回声、微钙化等特征对比差异有统计学意义($P<0.05$),见表1。

2.3 超声造影特征对比

恶性组的超声造影增强模式、强度与良性组对比差异都有统计学意义($P<0.05$),见表2。

2.4 造影灌注参数对比

恶性组的造影灌注参数PI、WIS、AUC值都高于良性组,TTP

表1 两组常规超声特征对比(例,%)

Table 1 Comparison of conventional ultrasound characteristics between two groups (n,%)

Groups	n	Shape (regular / irregular)	Edge (smooth/blurry)	Echo (hyperechoic/equivalent hypoechoic)	Microcalcification (Yes/No)
Malignant group	32	3/29*	3/29*	30/2*	30/2*
Benign group	116	55/61	76/40	39/67	12/104

Note: Compared with the benign group, * $P<0.05$.

值低于良性组,对比差异都有统计学意义($P<0.05$),见表3。

表2 两组超声造影特征对比(例,%)

Table 2 Comparison of ultrasound contrast characteristics between the two groups (n,%)

Groups	n	Enhanced intensity (high/low/equal enhancement)	Enhanced mode (fast in/out/ fast in/out/other)
Malignant group	32	24/6/2*	25/5/2*
Benign group	116	36/35/45	41/33/42

Note: Compared with the benign group, * $P<0.05$.

表3 两组超声造影灌注参数对比($\bar{x}\pm s$)

Table 3 Comparison of perfusion parameters of ultrasound contrast between two groups ($\bar{x}\pm s$)

Groups	n	PI(dB)	WIS	AUC	TTP(s)
Malignant group	32	8.89 $\pm$ 0.23*	7.98 $\pm$ 0.23*	405.92 $\pm$ 29.92*	17.78 $\pm$ 2.59*
Benign group	116	4.67 $\pm$ 0.25	6.98 $\pm$ 0.31	274.09 $\pm$ 28.01	34.67 $\pm$ 1.00

Note: Compared with the benign group, * $P<0.05$.

2.5 超声弹性成像组织弥散定量参数对比

SD、MEAN 值高于良性组,对比差异都有统计学意义($P<0.05$),

恶性组的组织弥散定量参数 %AREA 低于良性组, 见表4。

表4 两组超声弹性成像组织弥散定量参数对比($\bar{x}\pm s$)

Table 4 Comparison of quantitative parameters of tissue dispersion in two groups of ultrasound elastography ($\bar{x}\pm s$)

Groups	n	%AREA	SD	MEAN
Malignant group	32	18.87 $\pm$ 2.14*	43.28 $\pm$ 3.11*	112.76 $\pm$ 2.77*
Benign group	116	22.44 $\pm$ 1.34	34.28 $\pm$ 2.85	104.02 $\pm$ 3.22

Note: Compared with the benign group, * $P<0.05$.

3 讨论

乳腺癌是妇女最常见的恶性肿瘤之一,发病率年增加3%左右,在部分地区已位居女性恶性肿瘤的第一位,乳腺癌早发现、早诊断及早治疗是改善预后的关键^[3]。当前已有多种影像学可用于乳腺肿瘤的诊断,包括超声、CT、MRI、X线等,其中超声检查具有无辐射、实时方便、经济实用、无创等优点^[4,15]。本研究显示良性组与恶性组的超声病灶形状、边缘、回声、微钙化等特征对比差异有统计学意义,与郭瑾^[16]的研究类似,探讨乳腺癌三维超声血流参数与病理学指标的相关性,发现恶性组二维超声主要表现为病灶微钙化、回声衰减、侧方声影、内部回声不均匀、边界不清晰、形态不规则,与良性组对比差异有统计学意义,说明乳腺癌三维超声血流参数与病理学诊断有很好的相关性。从机制上分析,高回声对应的组织学特征是肿瘤细胞侵入周围脂肪组织并与脂肪细胞和弹性纤维相混合,多出现在病理分级较低以及有边缘模糊的肿瘤^[17]。微钙化也是乳腺癌的恶性特征之一,是其生长超过正常组织平面的结果^[18]。不过常规超声对早期乳腺癌的检出并不敏感,无法显示病灶内微循环特征。

超声造影是通过注射微泡作为造影剂使体内组织显影的方法,其能清晰显示乳腺肿瘤内新生微小血管的形态分布与分布状态,也能显示肿瘤内部及周边的低流量、低流速的微循环灌注情况^[19]。超声造影剂声诺维的微泡平均粒径2~4 μm ,浓度108/ml,具有良好的稳定性,不易在低声压下被振破,能产生良好的谐波信号,能获取低噪声下的实时谐波图像^[20]。本研究显

示恶性组的超声造影增强模式、强度与良性组对比差异都有统计学意义,与韩丕华^[21]等学者的研究一致,该学者研究超声造影对于乳腺癌腋窝良恶性淋巴结的诊断价值,结果显示恶性组的超声造影增强模式、强化时间与良性组对比差异都有统计学意义。TTP可反映超声造影过程中微泡的流动速度,PI可反映单位时间内进入病灶内的造影剂最大值,AUC是综合评价流量、时间、流速的指标,WIS可以反映造影剂进入病灶内血流速度的快慢,三者结合可清晰反映不同类型病灶造影模式的不同^[22]。从机制上分析,乳腺癌具有较为明显的恶性肿瘤特征,表现为高增强与快进快/慢退,良性肿瘤的造影特征却呈相反状态^[23]。主要在于乳腺癌的内部血管走行较为集中,且呈簇状或放射状的排列,这些肿瘤新生血管的管壁不同于正常血管管壁,管径较为粗大,管壁较薄且无正常肌层结构支撑、病灶部位存在大量迂曲微小血管,可促进肿瘤的发生与发展^[24]。良性肿瘤中多以乳腺腺病、导管内乳头状瘤、乳腺纤维腺瘤较为多见,病灶周边有稳定的微环境,病灶内具有走行良好成熟且稳定的正常血管,肿瘤组织分化良好,生长缓慢^[25,26]。

在乳腺肿瘤的早期诊断中,良性肿瘤与恶性肿瘤的超声鉴别特征在一定条件下并不典型,导致鉴别诊断比较困难^[27]。超声弹性成像组织弥散定量分析可客观评价组织软硬度的弹性参数,可使得超声诊断结果更加准确与全面^[28]。%AREA代表感兴趣内相对变形程度在阈值以下的像素占总像素的比例,%AREA值越大,代表组织越硬;MEAN代表感兴趣内相对变形的平均值,SD为相对偏差,两者值越小,代表组织越硬^[29,30]。本

研究显示恶性组的组织弥散定量参数%AREA 低于良性组, SD, MEAN 值高于良性组。与张晓彤^[31]等学者的研究类似, 该学者应用超声组织弥散定量分析技术检测乳腺癌术前 TAC 化疗者的肝脏组织弹性特征, 结果显示化疗后, MEAN 均减低, % AREA 增高, 说明%AREA 及 MEAN 有望成为定量检测 TAC 化疗乳腺癌患者早期肝脏损伤的有效指标。特别是当前超声弹性成像可以进入组织更深处, 并且有空化效应、热效应, 对于敏感的肿瘤细胞具有很好的诊断作用^[32,33]。本研究也有一定的不足, 收集的病例数相对较少, 样本含量少, 整理超声声像图表现时存在主观性, 将在后续研究中进行深入分析。

总之, 超声造影联合超声弹性成像组织弥散定量分析在乳腺癌诊断中的应用作为一种经济快捷、实时无创、重复性好的检查方法, 能够定量评估乳腺癌的影像学特征, 可为乳腺癌的临床治疗提供早期、确切的更多有价值的诊断信息。

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