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超声造影联合声触诊组织成像量化技术诊断乳腺癌前哨淋巴结的效能

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[摘要] 目的: 分析超声造影(contrast-enhanced ultrasound, CEUS)联合声触诊组织成像量化(virtual touch tissue imaging quantification, VTIQ)技术对乳腺癌前哨淋巴结(sentinel lymph node, SLN)的诊断效能。方法: 选取2018年4月至2021年2月江阴市中医院收治的104例(104个SLN)乳腺癌患者。术前均行CEUS及剪切波弹性成像检查分析SLN转移情况。以病理结果为金标准, 分析CEUS、剪切波速度(shear wave velocity, SWV)及联合诊断预测乳腺癌SLN转移的效能。结果: 术后病理证实104个SLN中转移性34个(转移性SLN组), 非转移性70个(非转移性SLN组)。转移性和非转移性SLN组的CEUS下SLN分型构成比比较, 差异有统计学意义($P < 0.05$), 此外VTIQ的SWV_{mean}比较, 差异亦有统计学意义($P < 0.05$); 将CEUS下I型归为非转移性SLN(-), II型及以上归为转移性SLN(+), 并与金标准(术后病理检查结果)比较, 得到的敏感度为88.2%(30/34)、特异度为71.4%(50/70); 绘制SWV_{mean}诊断转移性SLN的ROC曲线下面积为0.838, 最佳截断值为2.62 m/s, 敏感度、特异度分别为76.5%、82.8%; CEUS和VTIQ联合诊断转移性SLN的敏感度为94.1%(32/34)、特异度为91.4%(64/70)。结论: CEUS联合VTIQ对乳腺癌SLN转移具有较高的诊断效能, 提高了诊断准确率。

[关键词] 超声造影; 声触诊组织成像定量; 彩色多普勒超声; 乳腺癌; 前哨淋巴结

Efficacy of contrast-enhanced ultrasound combined with virtual touch tissue imaging quantification in the diagnosis of sentinel lymph node in breast cancer

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Abstract **Objective:** To analyze the diagnostic efficacy of contrast-enhanced ultrasound (CEUS) combined with virtual touch tissue imaging quantification (VTIQ) for sentinel lymph node (SLN) in breast cancer. **Methods:** A total of 104 breast cancer patients (104 SLNs) admitted to our hospital from April 2018 to February 2021 were selected. Preoperative CEUS and shear wave elastography were performed to analyze SLN metastasis. With pathological results as the gold standard, the efficacy of CEUS, SWV and combined diagnosis in predicting SLN metastasis in breast cancer was analyzed. **Results:** Among the 104 SLNs confirmed by postoperative pathology,

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34 were metastatic (metastatic SLN group) and 70 were non metastatic (non-metastatic SLN group). There was statistically significant difference in the proportion of SLN typing by CEUS between the metastatic group and the non-metastatic SNL group ($P<0.05$). In addition, compared with SWVmean of VTIQ, the difference was also statistically significant ($P<0.05$); type I under CEUS was classified as non-metastatic SNL (-), and type II and above were classified as metastatic SNL (+). Compared with the gold standard (postoperative pathological examination results), the sensitivity was 88.2% (30/34) and the specificity was 71.4% (50/70); the ROC curve of SMVmean for the diagnosis of metastatic SNL was drawn. The area under the curve was 0.838, the best cut-off value was 2.62 m/s, and the sensitivity and specificity were 76.5% and 82.8%, respectively. The sensitivity and specificity of CEUS and VTIQ in the diagnosis of metastatic SNL were 94.1% (32/34) and 91.4% (64/70). **Conclusion:** CEUS combined with VTIQ has high diagnostic efficiency for SLN metastasis of breast cancer, and improves the diagnostic accuracy.

Keywords contrast-enhanced ultrasound; virtual touch tissue imaging quantification; color Doppler ultrasound; breast cancer; sentinel lymph node

乳腺癌为常见女性恶性肿瘤, 严重威胁女性健康。前哨淋巴结(sentinel lymph node, SLN)为最先受肿瘤细胞浸润的淋巴结, 可对是否发生其他淋巴结的转移、乳腺癌分期、选择手术方式及评估预后等具有重要的提示作用。临床工作中探查和评估SLN十分重要^[1]。超声诊断技术因其便捷、经济等已成为术前诊断乳腺癌腋窝淋巴结的常用影像学方法, 但其缺点是敏感度、特异度低, 存在一定的误诊率和漏诊率^[2]。近年来随着影像技术的快速发展, 超声造影(contrast-enhanced ultrasound, CEUS)和超声弹性成像技术被逐渐应用于乳腺癌淋巴结的诊断^[3]。CEUS是利用造影剂使后散射回声增强, 反映不同组织的血流灌注情况, 有效弥补了常规超声的不足^[4]。声触诊组织成像量化(virtual touch tissue imaging quantification, VTIQ)为定量剪切波技术, 可提供多种弹性模式, 直观反映组织硬度信息^[5]。本研究拟探究CEUS及VTIQ预测乳腺癌SLN转移的价值。

1 对象与方法

1.1 对象

选取2018年4月至2021年2月江阴市中医院收治的乳腺癌患者, 共104例104个SLN。年龄31~76(47.9±9.1)岁。纳入标准: 1)年龄>18岁; 2)均为女性; 3)具有完整的术前超声检查(常规超声、CEUS及剪切波弹性成像检查)及病理结果资料。排除标准: 1)放化疗病史; 2)合并心、肝、肾等其他严重系统疾病; 3)合并全身感染性疾病及皮肤疾病。本次研究符合《世界医学协会赫尔辛基宣言》相关要求且所有患者均签署知情同意书。本研究经江阴市中医院医学伦理委员会批准

通过(审批号: LW2022011)。

1.2 仪器与方法

使用Philips iU22型超声诊断仪, L15探头(5~12 MHz), 探头配备对比脉冲序列造影成像技术且内置VTIQ软件。造影剂采用SonoVue冻干粉剂(意大利Bracco公司), 将其与5 mL 0.9%的氯化钠溶液振荡摇匀配制成微泡混悬液。1)超声造影: 患者取平卧位, 上臂外展90°, 暴露乳腺部位。先行二维超声检查, 观察病灶形态、大小、边界、内部回声、血流情况、纵横比、有无钙化、病灶周边组织及同侧腋窝淋巴结情况等, 此后将换能器切换至CEUS模式, 选择病灶最大切面作为超声造影观察切面, 确保焦点位于病灶后方, 固定探头, 用碘伏对乳晕周围皮肤进行消毒, 于乳晕周围皮下3、6、9、12点4个方向分别皮内注射0.3 mL SonoVue混悬液, 随即用5 mL 0.9%的氯化钠溶液冲管。启动对比脉冲序列双幅成像模式沿前哨淋巴通道追踪, 显影的第1个淋巴结为SLN, 记录其大小、部位及增强模式, 并于体表标记。CEUS的4种增强模式进行SLN分型。I型为均匀增强; II型为不均匀增强与高、低增强混合; III型为外周完全或不完全环状增强, 中心低或无增强; IV型为无增强或弱增强^[6](图1)。2)剪切波弹性成像: 对已标记的SLN启动VTIQ系统, 设置好感兴趣区(region of interest, ROI; 包括病灶及部分正常腺体组织), 嘱患者屏气, 按下“Update”按钮, 待图像稳定后定帧、存储, 同一病灶需采集三帧弹性图像, 获取VTIQ质量模式图和速度模式图。选择绿色质量模式图表示剪切波速度(shear wave velocity, SWV), 在绿色质量模式图像背景下, 转换成速度模式图。在图像中, SWV标尺为0~10 m/s, 当SWV分布均匀时, 在

淋巴结中选用6~10个取样框, 获取SWV值。然后计算其平均值(SWV_{mean}, 图2)。所有图像均经过至少2名高年资超声科医师独立审核, 结果不一致时经2人讨论后得出结论。

1.4 统计学处理

采用SPSS 21.0统计学软件分析数据。计

数资料以例(%)表示, 比较行 χ^2 检验或Fisher精确检验; 计量资料均符合正态分布, 以均数 \pm 标准差($\bar{x}\pm s$)表示, 比较行t检验。绘制受试者工作(receiver operating characteristic, ROC)曲线分析CEUS、VTIQ及联合诊断乳腺癌SLN转移的效能。 $P<0.05$ 为差异有统计学意义。

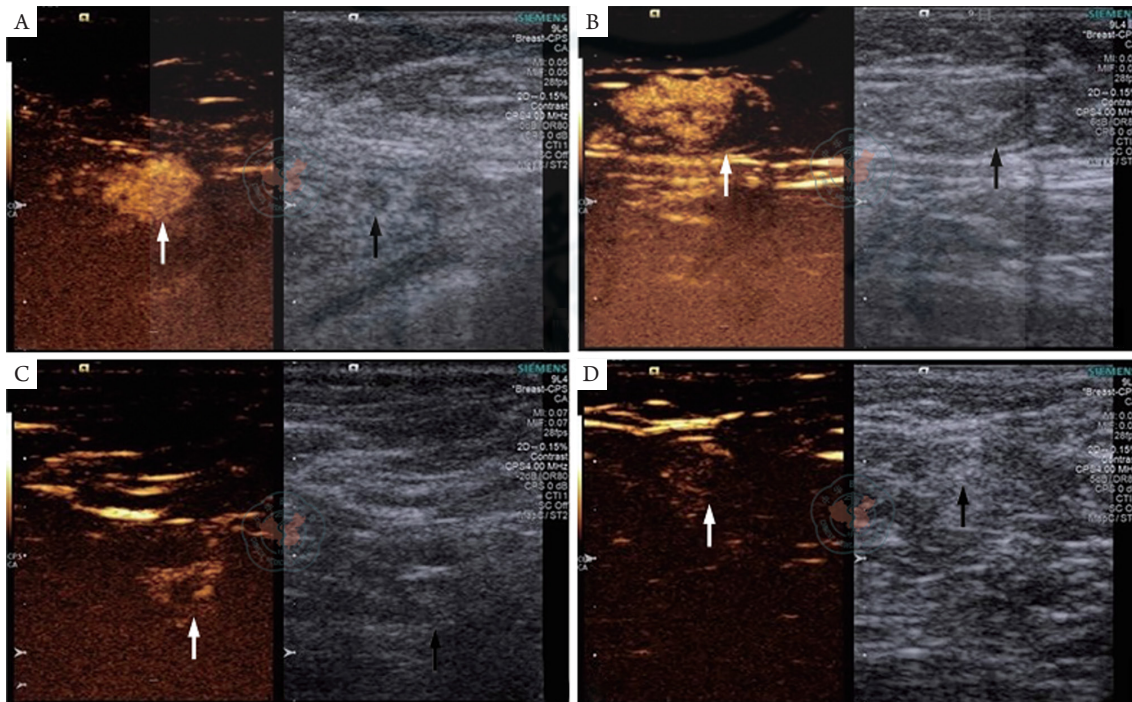


图1 CEUS下SLN分型

Figure 1 SLN typing by CEUS

白、黑箭头分别示CEUS及二维超声下淋巴结。(A)I型, 总体均匀增强; (B)II型, 可见不均匀增强; (C)III型, 见环形强化; (D)IV型, 为不强化或弱强化。

White and black arrows show CEUS and lymph nodes under two-dimensional ultrasound respectively. (A) Type I, with overall uniform enhancement; (B) Type II, with uneven enhancement; (C) Type III, with circular enhancement; (D) Type IV, with no or weak enhancement.

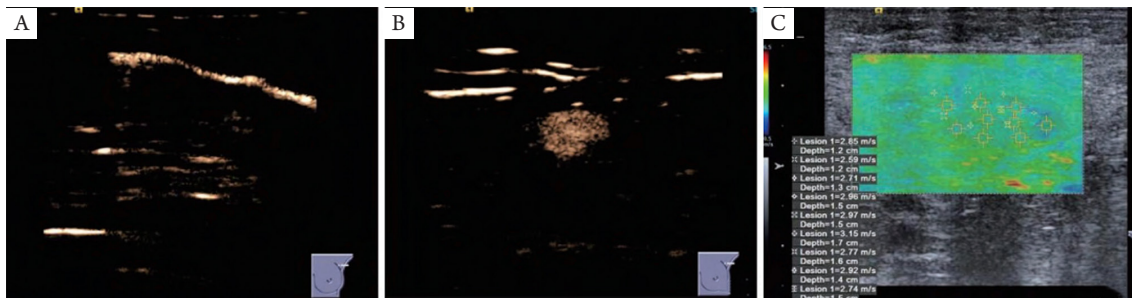


图2 患者, 女, 54岁, 左侧乳腺浸润性导管癌

Figure 2 A 54-year-old female patient with left breast invasive ductal carcinoma

(A)左侧乳腺淋巴管; (B)腋窝SLN; (C)VTIQ技术测量SLN的SWV。

(A) Left breast lymphatic vessels; (B) Axillary SLN; (C) SWV of SLN measured by VTIQ technology.

2 结果

2.1 转移性与非转移性 SNL 的一般资料比较

两组一般资料差异均无统计学意义(均 $P>0.05$, 表1)。

2.2 转移性与非转移性 SNL 的 CEUS 和 VTIQ 结果比较

术后病理证实104个SLN中转移性34个(转移性SNL组), 非转移性70个(非转移性SNL组)。注射造影剂10~20 s后, 淋巴管出现增强, 20 s~2 min 淋巴结从边缘区开始强化。转移性和非转移性

SNL的CEUS下SLN分型构成比比较, 差异有统计学意义($P<0.05$), 此外, VTIQ的SWVmean比较, 差异亦有统计学意义($P<0.05$, 表2)。

2.3 CEUS 诊断转移性 SNL 的效能分析

将CEUS下I型归为非转移性SNL(-), II型及以上归为转移性SNL(+), 并与金标准(术后病理检查结果)比较, 得到的敏感度为88.2%(30/34)、特异度为71.4%(50/70), 其中误诊20例, 漏诊4例(表3)。CEUS诊断转移性SNL的ROC曲线图见图3, AUC为0.829, 最佳截断值为1.5 m/s, 误诊20例, 漏诊4例。

表1 两组一般资料比较

Table 1 Comparison of general data between the 2 groups

组别	n	年龄/岁	直径/mm	病理分期/例			合并症/例		
				I	II	III	高血压	糖尿病	冠心病
转移性SNL	34	47.38 ± 8.72	46.79 ± 5.81	6	17	14	4	6	3
非转移性SNL	70	47.72 ± 9.01	45.97 ± 5.67	12	35	23	5	5	4
χ^2/t		0.158	0.589		0.268			0.308	
P		0.875	0.558		0.875			0.857	

表2 两组CEUS和VTIQ结果比较

Table 2 Comparison of CEUS and VTIQ results between the 2 groups

组别	n	CEUS/[例(%)]				VTIQ
		I型	II型	III型	IV型	SWVmean/(m·s ⁻¹)
转移性SNL	34	4 (11.8)	2 (5.9)	16 (47.1)	12 (35.3)	2.73 ± 0.58
非转移性SNL	70	50 (71.4)	16 (22.9)	4 (5.7)	0 (0.0)	2.15 ± 0.59
χ^2/t			8.392			4.728
P			0.004			<0.001

表3 对比CEUS检查与术后病理诊断转移性SNL的结果

Table 3 Comparison of CEUS examination and postoperative pathological diagnosis of metastatic SNL

CEUS检查	术后病理结果		合计
	+	-	
+	30	20	50
-	4	50	54
合计	34	70	104

2.4 VTIQ 诊断转移性 SNL 的效能分析

以SWVmean作为检验变量, 以病理结果(金

标准)作为状态变量(恶性=1, 良性=0), 绘制SWVmean诊断转移性SNL的ROC曲线(图4), 得曲线下面积为0.838, 最佳截断值为2.62 m/s, 敏感度、特异度分别为76.5%、82.8%, 约登指数为0.608, 其中误诊12例, 漏诊8例。

2.5 CEUS 和 VTIQ 联合诊断转移性 SNL 的效能分析

以CEUS下I型且SWVmean<2.62 m/s为非转移性SNL, 否则为转移性SNL, 对上述两项均不符合者以CEUS增强模式为标准进行判断。

与金标准(术后病理检查结果)比较,

CEUS和VTIQ联合诊断转移性SNL的敏感度为94.1%(32/34)、特异度为91.4%(64/70, 表4)。CEUS和VTIQ联合诊断转移性SNL的ROC曲线图见图5。AUC为0.957, 误诊6例, 漏诊2例。

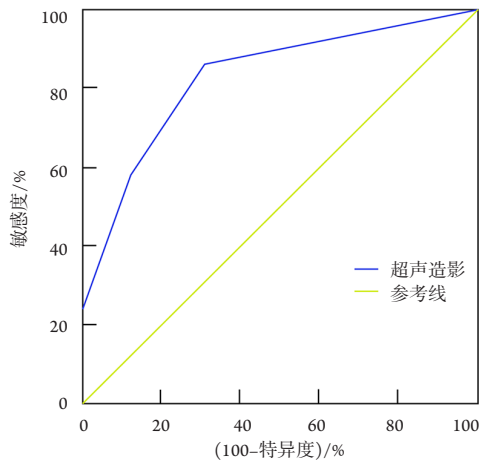


图3 CEUS诊断转移性SNL的ROC曲线

Figure 3 ROC curve of CEUS diagnosis of metastatic SNL

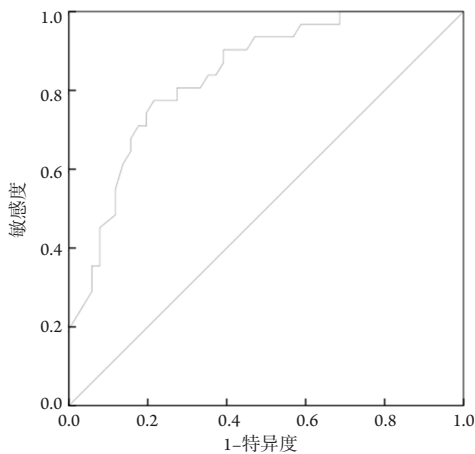


图4 VTIQ诊断转移性SNL的ROC曲线

Figure 4 ROC curve of VTIQ diagnosis metastatic SNL

表4 对比CEUS和VTIQ联合诊断与术后病理诊断转移性SNL的结果

Table 4 Comparison of combined diagnosis of CEUS and VTIQ and postoperative pathological diagnosis of metastatic SNL

CEUS和VTIQ 联合诊断	术后病理结果		合计
	+	-	
+	32	6	38
-	2	64	66
合计	34	70	104

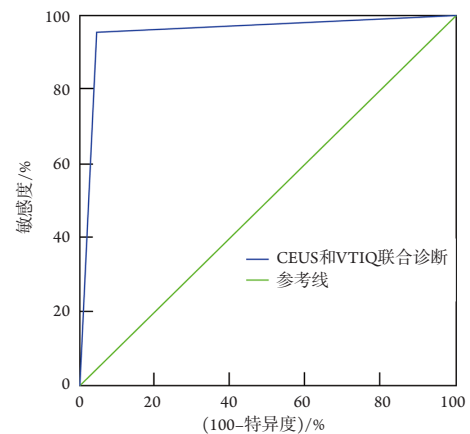


图5 CEUS和VTIQ联合诊断转移性SNL的ROC曲线

Figure 5 ROC curve of combined CEUS and VTIQ in the diagnosis of metastatic SNL

3 讨论

腋窝淋巴结的状态和分期是影响乳腺癌手术方案及预后的重要因素, 乳腺癌手术范围主要依靠SLN活检及冰冻切片检查来评估, 主要因为SLN最先接受原发肿瘤的淋巴引流, 即区域淋巴引流第1站, 是评估整个腋窝淋巴结受累状态的重要指标^[7-8]。临床多根据活检结果中SLN是否发生转移决定是否行腋窝淋巴结清扫。然而术中活检及冰冻切片需要专业病理医师评估, 这增加了手术的操作时间及治疗总成本^[9-10]。超声作为一项价格低廉、安全无创的检查方法, 近些年取得了长足的发展, 其用于术前淋巴结诊断已被临床广泛认可, 特别是CEUS及弹性成像等新超声技术的出现, 更多的超声技术被逐渐用于检查SLN^[11-12]。

CEUS是通过注射造影剂来增加不同组织之间的对比度以提高超声检查的显像能力^[13-14]。本研究结果显示: 转移性SNL和非转移性SNL的CEUS下SLN分型构成比明显不同, 以SNL呈I型增强预测非转移性SNL、II型及以上增强预测转移性SNL的效能, 敏感度为88.2%(30/34)、特异度为71.4%(50/70), 提示CEUS诊断转移性SNL的敏感度较高, 主要因为毛细淋巴管通透性强, 超声造影剂更容易进入毛细淋巴管显像^[15]。然而再检查中发现误诊20例, 漏诊4例, 主要为表现为II、III型强化, 这可能是由于组织反应性增生阻塞周边细小的淋巴管, 导致淋巴结不均匀强化, 当然也可能与医师的操作有关。

乳腺癌恶性肿瘤细胞侵犯其周边引流的腋窝淋巴结时导致淋巴组织密度增高、皮质增厚, SLN质地变硬^[16]。弹性成像技术是一种反映和测定组织形态学特征及硬度的新技术, 目前已应用

于乳腺癌腋窝淋巴结转移的诊断^[17-18]。VTIQ通过测量SLN的硬度信息判断乳腺癌是否发生淋巴结转移^[19-20]。本研究通过绘制VTIQ的定量参数SWVmean预测SLN转移的ROC曲线, 结果显示当SWVmean截断值取2.62 m/s, 得敏感度、特异度分别为76.5%、82.8%, 提示其鉴别SLN是否转移的特异度高但敏感度低, 其中误诊12例, 漏诊8例, 可能因淋巴结病变易受年龄、炎症等因素影响质地变硬。经CEUS和VTIQ联合诊断SLN转移的敏感度、特异度均高于单项技术, 因此可以认为联合诊断可提高乳腺癌淋巴结转移的诊断效能, 为乳腺癌术前腋窝淋巴评估提供可靠依据。

综上所述, CEUS联合VTIQ对乳腺癌SLN转移具有较高的诊断效能, 提高了诊断准确率。本研究不足之处在于, 受制于样本量及转移性淋巴结数目较少等可能使研究结果存在一定偏倚, 这有待后续增加样本量进一步验证该结论。

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