

• 综述 •

乳腺癌腋窝淋巴结转移的 MRI 评价*

张欣, 罗红兵 综述, 张剑辉, 刘圆圆[△] 审校

610041 成都, 四川省肿瘤医院·研究所, 四川省癌症防治中心, 电子科技大学医学院 乳腺外科中心 (张欣、张剑辉), 影像诊治部(罗红兵、刘圆圆)

[摘要] 乳腺癌是女性最为常见的恶性肿瘤之一, 腋窝淋巴结的转移情况对疾病分期、治疗手段的选择以及预后判断具有重要意义。现阶段临床多采用超声或前哨淋巴结活检来评价腋窝淋巴结有无转移, 但上述方法存在不足之处或伴随并发症的发生。MRI 近年来越来越多地运用于乳腺癌腋窝淋巴结转移的无创诊断。本文将回顾通过 MRI 直接评价乳腺癌腋窝淋巴结转移(而非通过肿瘤本身的 MRI 相关特征预测腋窝淋巴结转移)的文献, 并将 MRI 的相关特征用于诊断乳腺癌腋窝淋巴结转移的准确性进行综述。本文发现, 目前的研究结果之间存在差异, 使用 MRI 多参数联合或可提高诊断准确性, 并且影像组学的出现也为诊断带来了新的机遇。

[关键词] 乳腺癌; 磁共振成像; 腋窝淋巴结; 转移

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MRI Assessment of Axillary Lymph Node Metastases in Breast Cancer

Zhang Xin, Luo Hongbing, Zhang Jianhui, Liu Yuanyuan

Department of Breast Surgery, Sichuan Cancer Hospital & Institute, Sichuan Cancer Center, School of Medicine, University of Electronic Science and Technology of China, Chengdu 610041, Sichuan, China (Zhang Xin, Zhang Jianhui); Department of Medical Imaging, Sichuan Cancer Hospital & Institute, Sichuan Cancer Center, School of Medicine, University of Electronic Science and Technology of China, Chengdu 610041, Sichuan, China (Luo Hongbing, Liu Yuanyuan)

Corresponding author: Liu Yuanyuan, E-mail: lyyljj321@126.com

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[Abstract] Breast cancer has become one of the most common malignant tumors in women. The status of axillary lymph nodes metastases helps determine stages and surgical/post-surgical management of the disease, and remains one of the most important prognostic factors in breast cancer. At present, ultrasound or sentinel lymph node biopsy is often used to evaluate axillary lymph node metastases, but the above methods have shortcomings or may accompany complications. Magnetic resonance imaging (MRI) has been increasingly used in the noninvasive diagnosis of axillary lymph node metastases in breast cancer in recent years. We reviewed studies evaluating the use of MRI in detecting metastatic axillary lymph nodes in breast cancer patients (studies employing MRI characteristics of breast cancer to predict axillary lymph nodes metastases were not included), and summarized the diagnostic accuracy of MRI in discriminating metastatic axillary lymph nodes from nonmetastatic axillary lymph nodes. We found that results of studies were not consistent, and the diagnostic accuracy could be increased by combining morphological, dynamic and/or functional features on MRI; furthermore, the radiomics research would be of great potential and value in identifying metastatic lymph nodes.

[Key words] Breast cancer; MRI; Axillary lymph node; Metastasis

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[通讯作者] [△]刘圆圆, E-mail: lyyljj321@126.com

乳腺癌是女性最为常见的恶性肿瘤之一, 是引起女性死亡的重要原因^[1], 在我国更是呈年轻化、上升化趋势^[2-3]。乳腺癌腋窝淋巴结的转移情况对

疾病分期、治疗手段的选择以及预后判断有重要意义。目前临床多采用超声或前哨淋巴结活检来评价腋窝淋巴结有无转移。超声检查的优势在于无创、经济,但是对操作者依赖性强,对深部淋巴结的诊断较为困难^[4-5]。前哨淋巴结活检是临床上广泛推崇和应用的技术,部分取代了腋窝淋巴结清扫术,但有研究表明同腋窝清扫术后病理结果相比较,其灵敏度、特异度分别为 93%、100%,存在 9.8% 的假阴性率^[6-7],并且该技术仍为有创操作,可导致局部积液、淋巴水肿等并发症。

随着影像学方法和技术的发展,凭借无创、无辐射、优异的软组织分辨率等优点,MRI 被越来越多地运用于乳腺癌及其腋窝淋巴结转移的诊断^[8]。近年来,除常规 MRI,功能磁共振[如弥散加权成像(diffusion-weighted imaging, DWI)]也越来越多地得到重视及应用,并且可定量评估腋窝淋巴结转移。MRI 可能成为直接评价乳腺癌腋窝淋巴结转移(而非通过乳腺肿瘤本身的 MRI 相关特征预测腋窝淋巴结转移)的另一种手段,以尽量避免有创操作及其引发的并发症,并有利于个性化治疗方案的制定。

1 常规平扫 MRI 用于诊断乳腺癌腋窝淋巴结转移

常规平扫 MRI 上的定量或定性参数主要包括:腋窝淋巴结大小(长短径或长短径比值)、边缘、有无脂肪门、有无皮质不均增厚、有无淋巴结周围水肿。上述指标均对淋巴结转移有一定的预测作用:研究^[9-11]发现短径 >0.5 cm 或 1.0 cm 评价淋巴结转移的灵敏度介于 55% ~ 63%,特异度 80% ~ 86.7%;Razek 等^[12]将短径/长径比值 >0.6 用于判定淋巴结转移,灵敏度达 100%,特异度为 85.7%。单独运用无脂肪门判断淋巴结转移,其灵敏度不高,特异度介于 63.4% ~ 90.2%^[13-14]。有研究认为皮质厚度 >0.54 cm 高度提示淋巴结转移^[15]。多数研究将上述多个平扫特征综合起来用于评价淋巴结转移(包括短径 >1.0 cm、长径/短径 <1.5 、无脂肪门、皮质不均增厚、周围水肿),其灵敏度介于 23.1% ~ 66.7%,特异度介于 80% ~ 91%^[11, 16-20]。但也有部分研究结果与之矛盾,认为淋巴结的个数、短径或长短径比值与淋巴结转移不相关^[13-14, 21-22]。另外 Li 等^[23]对淋巴结 T2* 值的研究表明,转移淋巴结的平均 T2* 值长于未转移淋巴结,分别为 (55.96 ± 11.87) ms 和 (26.0 ± 5.51) ms;若将 37.5 ms 作为判断阈值,其具有较高的诊断灵敏度及特异度,分别为

94.6% 和 98.5%。总体来说运用 MR 平扫特征用于评价腋窝淋巴结转移的灵敏度不高,且部分研究结果之间存在不一致性。

2 增强 MRI 用于诊断乳腺癌腋窝淋巴结转移

2.1 钆剂动态增强 MRI

钆剂动态增强 MRI 用于判断淋巴结转移的定量及定性指标主要包括:强化率(强化第 4 期与第 1 期之间信号强度相比)、初始强化率(强化第 1 期与增强之前相比)、快速洗脱,时间信号强度曲线、曲线下面积及增强后高信号的缺失。Murray 等^[24]研究发现强化率 $>21\%$ 用于判定淋巴结转移的灵敏度为 100%,但特异性仅 41%。Kvistad 等^[11]研究发现初始强化率 $>100\%$ 的诊断灵敏度为 83%、特异度为 90%,快速洗脱的灵敏度也为 83%、但特异度仅 51%。而另一研究中,快速洗脱($>49\%$)具有较高的诊断灵敏度及特异度,分别为 84.9% 和 92.8%^[25]。He 等^[26]发现早期强化率 $>50\%$ 具有 97% 的诊断灵敏度、73.5% 的特异度,另外 II 型或 III 型时间信号强度曲线诊断灵敏度达 99.3%,但特异度仅为 60.7%;另一项研究也有类似发现:III 型时间信号强度曲线诊断灵敏度达 91.2%,但特异度仅为 68.8%^[27]。Fusco 等^[28]研究发现动力学特征中钆造影剂曲线下面积用于诊断淋巴结转移具有较高的准确度(75.8%)。Schipper 等^[29]运用增强后高信号的缺失用于诊断的特异度达 95%,但灵敏度仅 69%。而 Orgüç 等^[30]则认为动态增强的快速强化及洗脱特征不适用于诊断淋巴结转移。综上可以发现,各研究之间的灵敏度及特异度差异较大,仍需后续研究优化或验证以上研究结果。

2.2 超小超顺磁性氧化铁(ultrasmall superparamagnetic iron oxide, USPIO)增强 MRI

USPIO 增强 MRI 的相关研究主要是根据淋巴结摄取超顺磁性氧化铁(superparamagnetic iron oxide, SPIO)后信号的改变来判断淋巴结有无转移。若不均匀摄取或不摄取 SPIO,致影像上表现为增强后 T2* WI 上高信号或信号不均降低,判断为有淋巴结转移;反之均匀摄取 SPIO, T2* WI 上信号均匀降低,则无淋巴结转移。仅运用 SPIO 增强后的信号改变作为判断指标,其灵敏度及特异度均达到 100%,但其研究例数较少(分别为 10 例和 22 例)^[31-32]。而其它研究^[33-35]除了信号特征,还结合了淋巴结的大小、长短径、形态或有无脂肪门这些指标,其诊断灵敏度和特异度分别为 82% ~ 100%、80% ~

100%。最近的两篇 Meta 分析^[36-37]表明 SPIO 用于诊断淋巴结转移具有较高的灵敏度(分别为 83%、98%)及特异度(分别为 95.9%、96%)。虽然其用于诊断淋巴结转移,具有较高的诊断准确性,但由于目前商品化的 SPIO 已停产,在我国现阶段暂无法运用于临床。

3 DWI 用于诊断乳腺癌腋窝淋巴结转移

DWI 为近年来用于乳腺癌淋巴结转移研究较多的功能磁共振。研究中单独运用定性指标即 DWI 上高信号作为判断指标,其灵敏度为 45%~96%,特异度为 44%~98%^[13,17,20,22,38]。运用定量指标表现扩散系数值(apparent diffusion coefficient, ADC)判断淋巴结转移的灵敏度介于 75.9%~94.7%,特异度为 81%~100%,相较定性指标有所提高^[12-13,21,39-42]; Kim 等^[17]和 Fatma 等^[13]的研究更直观地表明将 DWI 高信号和 ADC 值结合起来,相较单独使用 DWI 高信号指标,灵敏度分别从 51.3%、96% 上升至 60%、98.4%,而特异度分别从 90%、85% 上升至 93.6%、95.1%。大部分研究中转移淋巴结的 ADC 值通常低于阴性淋巴结,判断阈值通常为 $<0.812 \sim 1.35 \text{ s/mm}^2$,而 ADC 阈值有所差异的原因可能与机器的场强(例如 1.5T 或 3.0T)及 b 值的选择有关(例如 $b = 0, 500 \text{ s/mm}^2$ 或 $b = 0, 500, 800 \text{ s/mm}^2$)。但 Kamitani 等^[22]的研究结果与之相反,转移淋巴结的 ADC 值大于阴性淋巴结,其阈值为 $>1.05 \text{ s/mm}^2$,作者提出这可能与乳腺癌不同的病理类型以及良性淋巴结是否发生炎性反应有关。最近发表的几项 meta 分析^[43-45]表明, DWI 和 ADC 值用于评价乳腺癌淋巴结转移的合并灵敏度分别为 83%、89% 和 85%,合并特异度分别为 82%、83% 和 83%,并推荐使用 $b = 0, 800 \text{ s/mm}^2$ 进行扫描以获得更高的诊断准确性。总体来说, DWI 和 ADC 值用于判断淋巴结转移具有较高的灵敏度及特异度,具有较好的应用前景。

4 影像组学用于乳腺癌腋窝淋巴结的研究

影像组学研究近年来备受关注,影像组学的发展也给乳腺癌精准诊疗带来了新的机遇。其原理是通过计算机辅助系统深度挖掘图像信息,全面提取病灶底层特征(如灰度、纹理和形状等图像固有特征)和语义特征(空间关系等高级特征)以及表达特征(基因相关)。目前关于乳腺癌的影像组学研究多数是针对乳腺肿瘤本身,对乳腺癌腋窝淋巴结的

研究相对较少。Schacht 等^[46]的研究是基于增强后的乳腺癌腋窝淋巴结 MRI 提取其形态特征和纹理特征,共提取了 28 个影像组学特征,从中筛选出 5 个影像组学标签,预测淋巴结转移的曲线下面积均大于 0.65,按曲线下面积(area under the curve, AUC)值从高到低排列分别是:方向梯度直方图的方差(AUC 值为 0.70)、相关性(0.69)、方差差异(0.68)、能量(0.66)和球形度(0.66)。Fusco 等^[28]等基于腋窝淋巴结动态增强 MR 图像,提取了一系列形态特征(包括紧密度、球形度、直径及体积等),发现形态特征中紧密度用于判断腋窝淋巴结转移的准确度最高(82.3%)。针对乳腺癌腋窝淋巴结的影像组学研究目前仍处于初期阶段,需要未来更多的研究发现更具特异性的影像组学标签,以利于影像精准诊断。

5 MRI 多序列及多参数联合应用诊断乳腺癌腋窝淋巴结转移

临床上乳腺 MRI 除外平扫,通常会结合钆剂增强扫描和(或)DWI,如果将多序列多参数结合起来,是否会有助于淋巴结转移的诊断? Murray 等^[24]的研究发现将淋巴结面积大小与强化特征结合起来作为判断标准,可将诊断特异度从 41% 提高到 54%,灵敏度不受影响,均为 100%。而 Kvistad 等^[11]的研究发现在淋巴结大小及形态这些特征基础上,加上快速强化、洗脱的强化特征,用其去评价淋巴结转移状态,可在不影响灵敏度(均为 63%)的情况下,将诊断特异性从 80% 提高至 93%。平扫联合 ADC 值和(或)DWI 上的高信号,部分研究表明联合运用后其灵敏度、特异度均有提高,甚至均可达到 100%^[12,20];而将平扫、增强扫描指标及 ADC 值三者结合起来,判断淋巴结转移的灵敏度为 100%,特异度为 83.3%^[47]。此外有几项研究^[21, 26, 48]采用评分体系来判别(将平扫及增强扫描多项指标一一评分,总评分大于 3 分、4 分或 4.5 分,即判断为淋巴结转移阳性),吴佩琪等^[48]的研究具有较高的灵敏度(95.3%)、但特异度较低(65.2%), Kim 等^[21]的研究中灵敏度较低(60%)、但特异度较高(90.1%),而 He 等^[26]的研究同时具有较高的灵敏度和特异度(分别为 92.5%、90.6%)。MR 多序列及多参数联合应用,可一定程度提高灵敏度和(或)特异度,而何种组合或评分体系可使诊断准确性达到最优,仍是现阶段亟待研究和完善的问题。

6 MRI 与超声及 PET/CT 用于诊断乳腺癌腋窝淋巴结转移的对比

文献报道超声诊断乳腺癌腋窝淋巴结转移的准确性不甚理想,其灵敏度介于 45.2%~100%,特异度介于 50%~89%^[49-51];最近的一篇 meta 分析表明超声造影的诊断灵敏度为 54%、特异度为 100%^[52]。另有两篇 meta 分析表明 PET/CT 诊断乳腺癌腋窝淋巴结转移灵敏度分别为 66%、64%,特异度均为 93%^[36, 53]。也有研究将 MRI 与以上一种或两种检查方法在同一研究中进行直接对比,发现 MRI 与超声和(或)PET/CT 之间诊断准确性相当,差异无统计学意义,PET/CT 联合 MRI 或超声可提高诊断效能^[54-57],另有 meta 分析表明 MRI 联合超声也具有较高的诊断效能^[58]。

7 总结与展望

综上,虽然多数研究表明传统 MRI 和(或)功能 MRI 可无创评估乳腺癌淋巴结转移,但仍存在以下问题:首先,部分研究结果存在不一致性;其次,目前的大多数研究为回顾性的研究,除了前哨淋巴结的相关研究,多数研究并未实现淋巴结的一一对应,而且部分研究并未对所有腋窝淋巴结进行观察分析,而是选取较大者或强化较明显者纳入分析,均有可能导致假阴性的发生;另外,研究设备(1.5T 或 3.0T)、扫描参数(例如 DWI 中 b 值的选择)及线圈(例如乳腺线圈或体表线圈)的选择,都会对研究结果造成影响。目前尚需要更进一步的研究(特别是大规模前瞻性的研究,并且在统一条件下进行)来验证这些检查方法及相关指标的准确性。通过多序列多参数结合、并且联合影像组学工具进行深层次特征数据挖掘, MRI 能为临床提供更多的信息。相信在不久的将来, MRI 有望成为乳腺癌腋窝淋巴结诊断的无创手段,甚至取代前哨淋巴结活检。

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