

# 乳腺癌预后指标的磁共振成像研究进展

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## 摘 要

乳腺癌是临床上最常见的恶性肿瘤, 预后的好坏依赖于早期诊断, 早期治疗。乳腺磁共振(Magnetic resonance imaging, MRI)因其灵敏度、分辨率高等优势在临床中广泛应用, 尤其是动态增强磁共振(Dynamic contrast enhanced MRI, DCE-MRI)联合扩散加权成像(Diffusion-weighted imaging, DWI)更是提高了乳腺癌的早期诊断率, 并以此为依据进行分期。乳腺癌的预后指标包括病理类型、分子分型、雌激素(estrogen receptor, ER)、孕激素受体(Progesterone receptor, PR)、人类表皮生长因子受体2(Human epidermal growth factor receptor 2, Her2)、肿瘤增殖指数(Ki67)、淋巴结转移、有无脉管癌栓等。近年来, MRI成像特点与预后指标的相关性的研究成为了热点。本文就近年来该领域的研究所取得的进展进行综述。

## 关键词

乳腺癌, 磁共振, 预后指标

# Research Progress of Magnetic Resonance Imaging in Prognostic Indicators of Breast Cancer

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## Abstract

Breast cancer is the most common malignancy in clinical practice. Prognosis depends on early di-

agnosis and early treatment. Magnetic resonance imaging (MRI) is widely used in the clinic because of its high sensitivity and high resolution. In particular, Dynamic contrast enhanced MRI (DCE-MRI) combined with diffusion-weighted imaging (DWI) improves the early diagnosis rate of breast cancer. The prognostic indicators of breast cancer include pathological types, molecular typing, estrogen receptor (ER), progesterone receptor (PR), human epidermal growth factor receptor 2 (human epidermal growth factor receptor 2, Her2), tumor proliferation index (Ki67), lymph node metastasis, presence or absence of vascular tumor thrombus, etc. In recent years, the research on the correlation between MRI imaging characteristics and prognostic indicators has become a hot spot. This paper reviews the research progress in this field in recent years.

## Keywords

Breast Cancer, MRI, Prognostic Indicators

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## 1. 引言

根据世界卫生组织(WHO)国际癌症研究机构(IARC)发布的关于 2020 年全球癌症负担的最新数据,乳腺癌的数量增加了 226 万,正式取代肺癌成为世界上最常见的癌症。此外,与其他常见癌症相比,乳腺癌的诊断年龄更年轻,诊断年龄中位数为 61 岁[1]。近年来,乳腺癌被认为是一种生物异质性肿瘤。它包括不同的病理类型、ER、PR、Her2 和 Ki67 的状态、分子分型、腋窝淋巴结转移和脉管癌栓,表现出不同的临床结果。乳腺影像学在乳腺癌的诊断中起着至关重要的作用,包括乳房钼靶、超声、MRI。近年来,MRI,尤其是 DCE-MRI 联合 DWI 受到临床医生的青睐。作为一种无创、高灵敏度的检查手段,MRI 已越来越多地应用于乳腺疾病的评估,包括良恶性病变的鉴别诊断、术前评估、预处理计划和疗效预测[2]。与乳腺超声、钼靶相比,MRI 检查的软组织分辨率和空间分辨率更高,其敏感性范围在 89%到 99%之间,但特异性从 47%到 97%不等[3]。乳腺 MRI 扫描不但能够较为清楚地显示病灶形态学特征,如大小、形态、边界、轮廓、肿瘤血管、信号强度等,还能够获得病灶相关的血流动力学特征,如强化时间、早期强化率、表观扩散系数(Apparent Diffusion Coefficient, ADC)值、时间-信号强度曲线(Time-signal Intensity Curve, TIC)等。乳腺癌的预后指标包括病理类型、分子分型、ER、PR、Her2、Ki67、淋巴结转移、有无脉管癌栓等。目前,MRI 影像学特征与预后因素的相关性分析是当前研究的热点。先前发表的研究也表明,DCE-MRI 结合 DWI 的影像学特征与分子分型、淋巴结转移和其他预后指标显著相关。相反,也有学者认为 DCE-MRI 结合 DWI 不能预测浸润性乳腺癌的分子亚型和淋巴结转移。因此,该领域的研究仍存在争议。

## 2. MRI 影像学特点与 ER、PR、Her2、Ki67 的相关性

激素受体状态、Her2、Ki67 是乳腺癌重要的预后指标,根据这些不同的预后指标的状态将乳腺癌非为 4 个类型:Luminal A 型、Luminal B 型、Her2 过表达型和三阴性乳腺癌(Triple negative breast cancer, TNBC) [4]。Luminal A 型患者预后最好,Luminal B 型次之,而 TNBC 预后最差[5]。单独以某一预后标志物(ER、PR、Her2、Ki67)研究其与预后的相关性报道较少,例如 ER、PR 阴性患者主要由组织学分级较差,结局和生存率较差的老年患者组成[6],PR 阴性患者与更大的肿瘤大小,更多的肿瘤滋养血管和更

高的核等级相关[7]。张琳琳[8]等人根据 MRI 检测结果, 分析乳腺癌磁共振征象与生物学行为和分子分型之间的关系认为分叶征与 ER、PR、HER-2 和 Ki67 的阳性表达以及阴性表达之间均不存在显著关系( $p > 0.05$ ), 毛刺特征与 ER 阳性表达以及阴性表达之间存在显著正相关关系( $p < 0.05$ ), 其中 ER 在毛刺和无毛刺中的阳性表达率分别为 87.50% 和 33.33%, 不均匀强化与 HER-2 和 Ki67 阳性表达以及阴性表达之间均存在显著正相关关系( $p < 0.05$ ), HER-2 在不均匀强化和均匀强化中的阳性表达率分别为 35.71% 和 16.67%; Ki67 在不均匀强化和均匀强化中的阳性表达率分别为 97.62% 和 77.78%。

### 3. MRI 影像学特点与分子分型的相关性

乳腺良性肿瘤在影像学表现上通常为边缘规则, 边界清楚的圆形肿块, 而乳腺癌则表现为边缘不规则, 边界不清, 并有毛刺征、分叶征。Luminal A 型和 Luminal B 型在 DCE-MRI 形态学上并无明显差异, 但是在腋窝淋巴结转移方面 Luminal B 型的阳性预测值高于 Luminal A 型[9]。Wu [10]等人分析了 300 例术前行了磁共振检查的乳腺癌患者, 发现 Luminal A 型和 Luminal B 型与 MRI 簇状钙化相关, 且更可能出现乳头侵犯和皮肤侵犯。这有赖于 MRI 对软组织良好的分辨率。在 DWI 中, 与 Luminal A 相比, Luminal B 的 ADC 值较低, 并且具有较高 Ki-67 增殖指数[11], Martincich 等人也证实了这一发现[12]。但是也有学者认为 DCE-MRI 联合 DWI 在预测乳腺癌免疫组织化学因子和分子亚型的表达方面是没有意义的, 但在鉴别乳腺癌高、低病理分级方面有较高的价值[13]。随着影像组学及计算机技术的发展, 用计算机辅助软件计算肿瘤的圆度来预测新诊断乳腺癌的侵袭性成为可能[14], 而且该研究还表明肿瘤圆度与 ER 和 PR 呈负相关, 与 Ki67 和组织学分级呈正相关, 且肿瘤圆度评分越高, Ki67 水平越高, 而 ER 和 PR 水平越低。

TNBC 是一种生物学上和临床上极具侵袭性的肿瘤, 与其他类型乳腺癌相比, 局部复发率和远处转移率增加[15]。尽管 TNBC 具有侵袭性, 但它可以在常规乳腺成像中模拟良性病变, 缺乏癌症的典型恶性特征。在乳房 X 光检查中, TNBC 通常表现为肿块, 边缘局限且无钙化[16] [17]。在超声检查中, TNBC 通常表现为规则形状的肿块, 边界清晰[18]。先前发表的论文描述了 TNBC 最典型的特征, 包括肿块状病变、边缘增强和 T2 加权序列的肿瘤内高信号[19] [20] [21]。此外, 与其他乳腺癌亚型相比, TNBC 在 DWI 上更可能具有更高的表观扩散系数(Apparent diffusion coefficient, ADC)值[12] [22]。Giuliana [23]等人的研究认为边缘强化是 TNBC 的独立危险因素, 并且有着更高的 ADC 平均值( $p = 0.011$ )。Shang [24]等人回顾分析 64 例经手术或活检病理证实为浸润性乳腺癌患者, 结果显示浸润性乳腺癌分子亚型间 ADC 值并无显著差异( $p > 0.05$ ), 而且与 ER、PR、Her2 均无明显差异( $p > 0.05$ ), 但 ADC 值与 Ki-67 的表达呈负相关( $r = -0.249$ ,  $p = 0.039$ )。Her2 过表达型的预后是仅次于 TNBC 的类型。与 Luminal 型不同的是, Her2 过表达型并不具有典型的具有恶性病变的形态, 其肿瘤边缘比较光滑, 且形状较规则[25], 这与 TNBC 相似, 这也解释了为什么这两种类型乳腺癌对化疗比较敏感[26]。另一个与其他类型不同的特点在 MRI 上 Her2 表现出更多的病灶, Richard 等人认为[27]术前 MRI 可能最有利于 Her2 过度表达的肿瘤患者, 因为该研究在对患者年龄、肿瘤大小和核分级进行控制后, Her2 过表达患者发生多个病灶的可能性是 Luminal A 型患者的 2.4 倍( $p = 0.016$ ), 皮肤和乳头受累的可能性为 1.7 倍( $p = 0.013$ ), 腋窝疾病的可能性为 1.9 倍( $p = 0.011$ ), 在 DWI 上, Her2 过表达型较其他类型有更低的 ADC 值, 依据以上影像学特征能较好的和其他类型区分出来。

### 4. MRI 影像学特点与腋窝淋巴结转移的相关性

腋窝淋巴结转移情况是乳腺癌另外一个非常重要的预后指标。腋窝淋巴结的评估是乳腺癌治疗的一个组成部分, 影响分期、治疗计划和总体预后。目前前哨淋巴结活检(Sentinel lymph node biopsy, SLNB)

是确定临床淋巴结阴性乳腺癌患者腋窝淋巴结受累情况的金标准。与腋窝淋巴结清扫相比, SLNB 有着并发症少、手术时间短等优势, 但是对于 SLNB 阴性的患者, 是否可以豁免 SLNB 成为中外学者讨论的热点。虽然先前的研究已经提出了术前识别淋巴结转移患者的方法[28], 但是到目前为止, 还并没有关于术前非侵入性鉴别 SLN 的确切指南。基于术前成像的前哨淋巴结状态信息, DCE-MRI 联合 DWI 被认为可以用来预测腋窝淋巴结转移的工具之一, 因为出现区域淋巴结转移的乳腺癌患者肿瘤血管较为丰富[29], 而 DCE-MRI 在评估血管方面有着显著优势, 并且在 DWI 中, ADC 值与淋巴管浸润有关, 而淋巴管浸润也与淋巴结转移密切相关[30]。虽然没有关于 MRI 上的肿瘤大小与 SLN 转移之间关系的研究, 但有报道称肿瘤大小与腋窝淋巴结有相关性, 当肿瘤大小从 10~25 mm 增加时, 腋窝淋巴结转移率也从 11%~36% 增加[31]。在 DCE-MRI 中, 肿瘤内部增强、边缘强化、肿瘤周围大量微血管生成都是腋窝淋巴结转移的独立预测因子[32] [33] [34], 这为临床预测腋窝淋巴结转移提供了依据。

## 5. MRI 影像学特点与乳腺癌病理类型的相关性

乳腺癌病理类型繁多, 临床以浸润性癌最为多见, 占乳腺癌的 85%, 其中又以浸润性导管癌、浸润性小叶癌和髓样癌多见。乳腺癌形态学特征与病理类型关系的研究国外在钼靶 X 线摄影方面报道较多目前在 MRI 方面报道较少, 一般认为浸润性导管癌在影像学上形态变化最多, 表现为边缘常出现浸润、毛刺或小分叶等恶性征象, 伴有导管原位癌成分的浸润性导管癌常有钙化。而浸润性小叶癌在早期无明显肿块出现, 结构扭曲是浸润性小叶癌的一个常见征象, 微小钙化少见。来自国内的一项小样本临床研究表明[35], 浸润性导管癌及浸润性小叶癌多呈分叶形或不规则形, 边缘不规则或可见毛刺征, 而髓样癌多呈类圆形, 边缘光滑。在特殊类型癌中, 粘液癌表现出分叶状, T2WI 序列呈明显高信号, 而其他类型癌例均未见特征性影像学表现。

## 6. 结语

综上, 乳腺 MRI, 特别是 DCE-MRI 联合 DWI 在影像学特征上与乳腺癌预后指标, 包括 ER、PR、Her2、Ki67、分子分型、腋窝淋巴结及病理类型的相关性, 虽然目前仍存在较多争议且无明确的指南, 而且病理活检仍然是目前诊断的金标准, 但在侵入性操作之前如果能早期预测特定的预后指标将给后续的治疗方案提供帮助, 随着研究的深入及影像学的发展, 相信未来 MRI 在乳腺癌的诊断中将有着越来越重要的地位。

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