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Ki67 与 MRI 在宫颈癌根治性手术后宫颈癌淋巴结转移中评价对比 *

周满远 田忠甫 顾海磊 程 晖 何昌荣 唐文伟[△]

(南京医科大学附属妇产医院放射科 江苏 南京 210000)

摘要 目的:探究 Ki67 与 MR 在宫颈癌根治术后宫颈癌淋巴结转移中评估价值的对比。**方法:**选择 2016 年 1 月至 2018 年 1 月于我院接受宫颈癌根治术的 151 例宫颈癌患者,分别对其实施 Ki67 检测及 MRI 检测,以病理学检测结果为金标准,计算两种检测方式对宫颈癌淋巴结转移评估的准确度、敏感度、特异度、阳性预测值及阴性预测值,并进行对比分析。**结果:**检测评估发现,MRI 对宫颈癌淋巴结转移评估准确度为 31.79%,灵敏度为 46.75%,特异度为 16.22%,阳性预测值为 36.73%,阴性预测值为 22.64%。Ki67 检测对宫颈癌淋巴结转移评估准确度为 42.38%,灵敏度为 52.56%,特异度为 31.51%,阳性预测值为 45.05%,阴性预测值为 38.33%。两种检测方式对比显示 Ki67 对宫颈癌淋巴结转移具有更高的诊断准确度。**结论:**3 相比于 MRI 检测,Ki67 对宫颈癌淋巴结转移具有更高的诊断准确度、特异度和阴性预测值,分析其原因与 MRI 检测受个体因素影响更大有关。

关键词:Ki67;MRI;宫颈癌根治术;淋巴结转移

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Evaluation and Comparison of Ki67 and MRI in Lymph Node Metastasis of Cervical Cancer after Radical Operation of Cervical Cancer*

ZHOU Man-yuan, TIAN Zhong-fu, GU Hai-lei, CHENG Hui, HE Chang-rong, TANG Wen-wei[△]

(Department of radiology, Nanjing Medical University Maternity Hospital, Nanjing, Jiangsu, 210000, China)

ABSTRACT Objective: To explore the value of Ki67 and MRI in evaluating lymph node metastasis of cervical cancer after radical operation of cervical cancer. **Methods:** 151 patients with cervical cancer who underwent radical operation of cervical cancer in our hospital from January 2016 to January 2018 were selected as the research objects, and Ki67 and MRI were tested respectively, and the pathological results were used as the gold standard to calculate the two methods for evaluating lymph node metastasis of cervical cancer. Accuracy, sensitivity, specificity, positive predictive value and negative predictive value were compared and analyzed. **Results:** Testing and evaluation found that the accuracy of MRI for cervical cancer lymph node metastasis assessment was 31.79%, sensitivity was 46.75%, specificity was 16.22%, positive predictive value was 36.73%, and negative predictive value was 22.64%. The Ki67 test has an accuracy of 42.38%, a sensitivity of 52.56%, a specificity of 31.51%, a positive predictive value of 45.05%, and a negative predictive value of 38.33%. The comparison of the two methods showed that Ki67 had higher diagnostic accuracy for lymph node metastasis of cervical cancer. **Conclusion:** Compared with MRI, Ki67 had higher diagnostic accuracy, specificity and negative predictive value for lymph node metastasis of cervical cancer. Individual factors are more relevant.

Key words: Ki67; MRI; Radical resection of cervical cancer; Lymph node metastasis

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前言

宫颈癌是妇科常见恶性肿瘤之一,其发病率仅次于乳腺癌,位居女性恶性肿瘤发病率第二位^[1],近些年,随着近些年居民生活方式与起居习惯的改变,宫颈癌的发病率呈现逐年上升趋势^[2,3],统计数据显示,全球每年新增宫颈癌患者约为 50 万例,死亡例数约为 23.1 万例,我国每年宫颈癌新发病例高达 13.15 万,其发病率与死亡率均位居国内女性恶性肿瘤之首^[4,5]。

病毒感染、多次分娩、吸烟等因素都可能会诱发宫颈癌,且由于早期宫颈癌临床症状不明显,多数患者在发现时宫颈癌已发展至中后期,现阶段对宫颈癌的治疗主要包括手术治疗、化学治疗与放射治疗等^[6,7]。宫颈癌根治术能够显著缓解患者临床症状,但临床实践发现,部分女性术后会出现淋巴结转移情况,影响其术后恢复^[8]。准确的诊断对淋巴结转移的治疗具有重要意义,Ki67 是临床上用于反映细胞增殖活性的指标,也是目前较为肯定的核增殖标志基因^[9,10]。MRI 在临床上常被用于恶性肿

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作者简介:周满远(1987-),男,本科,住院医师,研究方向:妇科肿瘤,乳腺疾病,MRI 相关临床研究,

电话:13814064789,E-mail:zhoumanyuan1987@126.com

[△] 通讯作者:唐文伟(1971-),男,本科,主任医师,研究方向:女性生殖系统、乳腺和胎儿、婴幼儿影像学,

电话:13813889017,E-mail:tw3077@163.com

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瘤的诊疗中,但对该方式在肿瘤淋巴结转移中的报道较少。我们通过研究发现,相比于 MRI 检测, Ki67 对宫颈癌淋巴结转移具有更高的诊断准确度, 分析其原因与 MRI 检测受个体因素影响更大有关, 所以研究 Ki67 与 MRI 在宫颈癌根治性手术后宫颈癌淋巴结转移中的应用价值, 对临床早期发现、早期诊断宫颈癌具有十分重要的意义, 现详述如下。

1 资料与方法

1.1 一般资料

选择 2016 年 1 月至 2018 年 1 月于我院接受宫颈癌根治术的 151 例宫颈癌患者, 患者年龄 33-67 岁, 平均年龄 (46.32±2.51) 岁, 病程 1~5 年, 平均 (3.23±0.34) 年。纳入标准: (1) 均经病理学检测确诊; (2) 能够配合治疗; (3) 病历齐全; (4) 获得我院伦理学会批准; (5) 患者知情同意。排除标准: (1) 合并精神疾患者; (2) 合并其他恶性肿瘤者。

1.2 方法

所有入组对象均分别实施 Ki67 及 MRI 检测, Ki67 检测方式如下: 采集两组患者宫颈癌组织, 使用苏木素 - 伊红染色, 采用 SP 法染色, 具体操作步骤严格按照采购试剂盒进行, 组织样本采集后进行切片、烤片、脱蜡、水化、修复、画线、上机、DAB 显色、苏木素复染、干燥后使用显微镜进行结果观察; MRI 检测

选择飞利浦 1.5T、16 通道 MRI 实施, 设定层厚 5 mm、层间距 1 mm, 对宫颈部位实施平扫, 平扫结束后为患者注射 15 mL 对比剂, 流速为 2.0 mL/s, 注射后的 15 s、30 s、60 s 分别实施一次扫描, 层厚设置为 2.5 mm, 层间距设置为 0 mm。

1.3 观察指标及评测标准

1.3.1 Ki67 检测阳性判断标准 Ki67 阳性判别标准以细胞核内染色为准, 如观察区内细胞核内染色呈现棕黄色颗粒细胞所占比例 <10 %, 即为阴性, ≥ 10 % 即为阳性^[1]。

1.3.2 MRI 检测阳性判断标准 MRI 检测阳性判别标准为如 DWI 呈现稍高信号, 淋巴结 T2WI-TRA 短径 ≥ 1 cm, 即为阳性^[2]。

1.4 统计学方法

使用 SPSS24.0, 计数资料以 (%) 的形式表示, 采用卡方检验, 以 $P < 0.05$ 有统计学意义。

2 结果

2.1 Ki67 检测对淋巴结转移诊断结果判别

以病理学检测结果为金标准, 经计算判断, Ki67 检测对宫颈癌淋巴结转移评估准确度为 42.38 %, 灵敏度为 52.56 %, 特异度为 31.51 %, 阳性预测值为 45.05 %, 阴性预测值为 38.33 %, 具体数据如表 1 所示。

表 1 Ki67 检测对淋巴结转移诊断结果判别

Table 1 Ki67 detection for the diagnosis of lymph node metastasis

Ki67 diagnosis	Pathological diagnosis		Total
	Transfer	Non-transfer	
Transfer	41	50	91
Non-transfer	37	23	60
Total	78	73	151

2.2 MRI 检测对淋巴结转移诊断结果判别

以病理学检测结果为金标准, 经计算判断, MRI 对宫颈癌淋巴结转移评估准确度为 31.79 %, 灵敏度为 46.75 %, 特异度

为 16.22 %, 阳性预测值为 36.73 %, 阴性预测值为 22.64 %, 具体数据如表 2 所示。

表 2 MRI 检测对淋巴结转移诊断结果判别

Table 2 MRI detection for the diagnosis of lymph node metastasis

MRI diagnosis	Pathological diagnosis		Total
	Transfer	Non-transfer	
Transfer	36	62	98
Non-transfer	41	12	53
Total	77	74	151

2.3 两种检测方式对淋巴结转移判别能力对比

经评估对比发现, 相比于 MRI 检测, Ki67 检测具有更高的

评估准确度、特异度及阴性预测值, 具体数据如表 3 所示。

表 3 两种检测方式对淋巴结转移判别能力对比

Table 3 Comparison of two detection methods for discriminating lymph node metastasis

Detection method	n	Accuracy	Sensitivity	Specificity	Positive predictive value	Negative predictive value
Ki67	151	42.38%	52.56%	31.51%	45.05%	38.33%
MRI	151	31.79%	46.75%	16.22%	36.73%	22.64%

3 讨论

宫颈癌是发病率仅次于乳腺癌的女性恶性肿瘤,据世界卫生组织国际癌症研究署(IARC)报道,全球每年新发宫颈癌约有 53 万例,占有癌症发病例数的 5%,而发展中国家宫颈癌发病率显著高于发达国家^[13,14]。数据显示,我国每年宫颈癌发病例数约占全球新发病例的 28.8%,居我国妇女恶性肿瘤第一位,近些年随着居民生活方式的改变及饮食结构的调整,宫颈癌呈现年轻化趋势,给女性身心健康带来较大的威胁^[15]。宫颈癌根治术是宫颈癌最重要的治疗方式之一,适用于能够耐受手术、临床分期为早中期的患者,治疗后患者临床症状会得到显著改善,同时延长患者生存期^[16]。淋巴结术后转移是指肿瘤术后浸润的肿瘤细胞穿过淋巴管壁,随淋巴液被带至淋巴结,而后以此为中心生长出新肿瘤的现象,淋巴结术后转移是肿瘤复发的一种,会直接影响肿瘤患者的治疗进程,甚至导致治疗失败^[17]。调研显示,宫颈癌无淋巴结转移患者 5 年存活率为 87.5%,而存在淋巴结转移者 5 年存活率低至 49.7%,提示有效干预及诊断淋巴结转移对提高宫颈癌患者预后具有重要意义^[18]。

近些年随着分子生物学的发展,越来越多与肿瘤预后相关的生物学指标被应用于临床,如凋亡相关基因、增殖相关基因、转移相关基因等,Ki67 是临床上较具有代表性的指标,目前被广泛应用于各类恶性肿瘤增殖活性研究中^[19]。研究发现 Ki67 与多种肿瘤疾病的发生发展均具有较为密切的关联,如卵巢癌、淋巴瘤等,免疫组化对 Ki67 的检测结果显示能够应用于恶性肿瘤的诊断、治疗及疗效评估中^[20];也有研究通过将宫颈癌、宫颈上皮内瘤变及宫颈炎组织进行对比分析的方式发现,宫颈癌中 Ki67 表达阳性率明显高于上皮内瘤变及宫颈炎组织^[21],同时进一步分析显示 Ki67 表达与宫颈癌的临床分期、组织学分化程度有密切联系,推测该指标可以作为判别宫颈癌预后的标准^[22,23]。MRI 是临床上常用的影像学检查手段,在恶性肿瘤评估中也发挥重要作用,能够较好的反映宫颈癌的形态、大小、信号变化等特点^[24],对肿瘤性质的判别具有重要的参考,尤其是对内生性宫颈癌患者,MRI 能够显示难以明确的诊断区域病变状态,DWI 可以显示宫颈结构的结节或肿物,为诊断提供依据;学者 Fu L^[25]等的研究也指出,MRI 检测能够提供宫颈癌病理分型、分级、周围组织受累状态等情况,而进一步的增强扫描能够根据恶性肿瘤病变程度显现不同影像学特征。

我们通过对 151 例行宫颈癌根治术患者病历资料的回顾性分析,就 Ki67 级 MRI 在术后患者淋巴结转移中的判别价值进行了对比分析,结果显示,MRI 对宫颈癌淋巴结转移评估准确率为 31.79%,灵敏度为 46.75%,特异度为 16.22%,阳性预测值为 36.73%,阴性预测值为 22.64%,Ki67 检测对宫颈癌淋巴结转移评估准确率为 42.38%,灵敏度为 52.56%,特异度为 31.51%,阳性预测值为 45.05%,阴性预测值为 38.33%,同时组内比较发现,相比于 MRI 检测,Ki67 检测具有更高的评估准确度、特异度及阴性预测值。我们分析认为,宫颈癌根治术后的恢复情况是决定患者预后的重要因素,而早期对是否会出现淋巴结转移的预测能够为后期治疗方案的确定提供重要信息,MRI 检测能够较好的现实宫颈癌病灶大小、形态等基本特征。相比于正常组织,肿瘤组织中细胞密度较高、细胞间隙较小、细

胞质相对比例增加,因而其 AUC 值较小^[26],同时随着肿瘤恶性程度的增加,其细胞密度也会升高,提示 AUC 值与肿瘤恶变程度呈负相关联系,这说明在鉴别恶性肿瘤中 MRI 具有较好的应用价值。同时淋巴管转移是宫颈癌转移的重要途径,而宫颈基质环的完整性是反映癌细胞是否出现浸润的重要标志,如果基质环被破坏,则提示已出现宫旁浸润^[27,28]。Ki67 在宫颈癌评估中的应用已得到广泛认可,因该因子活跃于细胞周期所有阶段,但会随细胞周期而出现变化,在 G1 及 S 期早期表达较低,在 S 期及 G2 期会出现剧增,M 期达到顶峰,该特性使其能够成为标志细胞增殖的特异性物质^[29,30],本文研究结果就显示当宫颈癌细胞出现淋巴结转移后,其 Ki67 表达阳性率会出现明显上升。文中就两种检查方式对宫颈癌淋巴结转移判别效果进行了对比,结果显示 Ki67 检测准确度、特异度及阴性预测值更高,分析其原因与 MRI 检测一定程度上会受个体因素影响,而 Ki67 作为特异性的肿瘤标志物,其检测的独特性更高,也更为准确。

总而言之,相比于 MRI 检测,Ki67 对宫颈癌淋巴结转移具有更高的诊断准确度、特异度和阴性预测值,分析其原因与 MRI 检测受个体因素影响更大有关。

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