doi: 10.13241/j.cnki.pmb.2020.01.031

吲哚菁绿联合亚甲蓝在子宫内膜癌术中前哨淋巴结识别中的应用价值 *

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摘要 目的:探究吲哚菁绿联合亚甲蓝在子宫内膜癌术中前哨淋巴结识别中的应用价值。**方法:**选取2016年8月~2017年9月我院收治的子宫内膜癌患者93例,采用随机数字表法分为两组。对照组将亚甲蓝蓝染的淋巴结作为前哨淋巴结,观察组在对照组的基础上使用吲哚菁绿,蓝染和荧光显影的淋巴结作为前哨淋巴结。比较两组患者的前哨淋巴结切除时间、术中出血量、淋巴结切除数量、主动脉旁淋巴结切除例数、前哨淋巴结识别成功率,并比较两种方法的准确率、敏感性和特异性。术后随访12个月,对两组患者的复发情况和相关并发症进行比较。**结果:**两组患者的前哨淋巴结切除时间、术中出血量、淋巴结切除数量和主动脉旁淋巴结切除例数比较均无统计学差异($P>0.05$);观察组的前哨淋巴结识别成功率、准确率和特异性均显著高于对照组($P<0.05$),两组敏感度、复发率比较均无统计学差异($P>0.05$)。两组在随访期间均未发生皮肤坏死、过敏或永久性着色等相关不良反应。**结论:**吲哚菁绿联合亚甲蓝在子宫内膜癌术中识别前哨淋巴结的应用价值显著高于单用亚甲蓝。

关键词:吲菁绿;亚甲蓝;子宫内膜癌;前哨淋巴结识别

中图分类号:R737.33 **文献标识码:**A **文章编号:**1673-6273(2020)01-140-04

Application Value of Indorquine Green Combined with Methylene Blue for the Sentinel Lymph Node Identification in the Endometrial Carcinoma*

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ABSTRACT Objective: To explore the application value of indorquine green combined with methylene blue in sentinel lymph node identification for endometrial carcinoma. **Methods:** 93 cases of endometrial cancer patients admitted in our hospital from August 2016 to September 2017 were selected and divided into two groups by the random number table method. The methylene blue was used in the control group, indorquine green and methylene blue were used in the observation group. The sentinel lymph node excision time, intraoperative blood loss, number of lymph node excision, number of cases of para-aortic lymph node resection, sentinel lymph node identification rate were compared between two groups. And the accuracy, sensitivity and specificity of the two methods were also compared. All the patients were followed-up for 12 months, the relapse and incidence of related complications were compared between two groups. **Results:** There was no statistically significant difference in the sentinel node resection time, intraoperative blood loss, number of lymph node resection and number of para-aortic lymph node resection cases between the two groups ($P>0.05$). The success rate of sentinel node recognition, accuracy and specificity of the observation group was significantly higher than that of the control group ($P<0.05$), and there was no statistical difference in the sensitivity and recurrence rate between the two groups ($P>0.05$). No adverse reactions such as skin necrosis, allergy or permanent staining occurred in either group during the follow-up period. **Conclusion:** The application value of indoturnip-green combined with methylene blue in the identification of sentinel lymph nodes in endometrial cancer is significantly higher than that of methylene blue alone.

Key words: Indorquine green; Methylene blue; Endometrial carcinoma; Sentinel lymph node identification

Chinese Library Classification(CLC): R737.33 Document code: A

Article ID: 1673-6273(2020)01-140-04

前言

子宫内膜癌是妇科常见的恶性中肿瘤之一,其发病率呈现逐年上升的趋势,约占妇科生殖道肿瘤的30%,居女性恶性肿瘤的第6位[1-3]。子宫内膜癌临床主要表现为阴道不规则出血,多数患者确诊时为早期[4]。早期子宫内膜癌主要采用手术治疗,包括子宫广泛切除术或联合盆腔和腹主动脉旁淋巴结清扫术,但手术范围目前尚未形成统一的标准[5,6]。子宫内膜癌患者的淋巴结转移直接影响预后。有研究显示无淋巴结转移的患者5年生存期达90%,淋巴结转移阳性的5年生存期仅为54%[7-9]。但

* 基金项目:广西壮族自治区教育厅基金项目(GKE2017-KF06)

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(收稿日期:2019-03-27 接受日期:2019-04-23)

也有研究认为早期子宫内膜癌的淋巴结转移率仅为 10%,大范围淋巴结清扫可能会引起术后淋巴囊肿、下肢淋巴水肿等并发症,还会损伤免疫系统,对患者的生活质量造成影响[10-12]。因此,淋巴结清扫范围的确定对于患者的预后至关重要。

前哨淋巴结是原发肿瘤转移的第一道淋巴结,如果前哨淋巴结没有发生转移则其后的淋巴结可以认为未被侵犯[13-15]。选择性切除淋巴结可降低早期子宫内膜癌患者的检测选择性对淋巴结进行切除,以降低患者的手术、麻醉风险和并发症的发生率,提高患者的生活质量[16,17]。本研究主要分析了吲哚菁绿联合亚甲蓝对子宫内膜癌术中前哨淋巴结识别的价值,旨在为临床手术范围的确定提供参考依据。

1 资料和方法

1.1 一般资料

选择 2016 年 8 月 ~2017 年 9 月我院收治的 93 例子宫内膜癌患者,均符合子宫内膜癌的相关诊断标准。纳入标准:① 子宫内膜癌Ⅰ期;② 无盆腹腔淋巴结切除史;③ 入组前未接受放化疗治疗;④ 患者知情同意并签署知情同意书。排除标准:① 合并其他恶性肿瘤者;② 术前 CT 和 MRI 检查未发现淋巴结肿大者;③ 对本研究所用试剂过敏;④ 合并其他重要器官功能障碍。采用随机数字表法将患者分为两组,对照组 46 例,年龄 38~65 岁,平均 55.85± 5.12 岁;病理类型:内膜样腺癌 42 例,腺角化癌 2 例,透明细胞癌 1 例,浆液性腺癌 1 例;分化程度:高分化 27 例,中分化 13 例,低分化 6 例。观察组 47 例,年龄 40~65 岁,平均 56.33± 5.54 岁;病理类型:内膜样腺癌 42 例,腺角化癌 2 例,透明细胞癌 2 例,浆液性腺癌 1 例;分化程度:高分化 26 例,中分化 14 例,低分化 7 例。两组一般资料比较差异均无统计学意义(P>0.05),具有可比性。

1.2 治疗方法

患者取截石位,采用全身静脉麻醉,于脐下做 1 cm 切口,并建立 CO_2 气腹,置入腹腔镜,探查患者的腹内及盆腔情况。腹腔镜下在子宫体 3、6、9 和 12 点的位置距肿瘤病灶边缘 0.5 cm 以上分别注射亚甲蓝 (西南药业股份有限公司, 国药准字 H50020129)1 mL (1%),深度为 1 cm。对照组将蓝染的淋巴结作为前哨淋巴结,并记录前哨淋巴结的位置和数量。观察组在对照组的基础上于宫颈粘膜下层 0.3~0.5 cm 处注射 2 mL (1 mg/mL) 吲哚菁绿 (丹东医创药业有限责任公司, 国药准字 H20073073),在红外线下将荧光显影的淋巴结和蓝染的淋巴结作为前哨淋巴结。两组患者均在腹腔镜下切除蓝染和荧光显影确定的前哨淋巴结,并行广泛子宫切除术联合盆腹腔淋巴结切除术。术中快速冰冻切除的前哨淋巴结并送病理检查。

1.3 观察指标

① 术中相关指标,包括前哨淋巴结切除时间、术中出血量、淋巴结切除数量和主动脉旁淋巴结切除例数。② 前哨淋巴结识别成功率。③ 准确率、灵敏度和特异性。真阳性:术中诊断为前哨淋巴结且术后病理检查显示有癌细胞转移;真阴性:术中诊断为非前哨淋巴结且术后病理检查显示无癌细胞转移; 假阳性: 术中诊断为前哨淋巴结但术后病理检查显示无癌细胞转移;假阴性:术中诊断为非前哨淋巴结但术后病理检查显示有癌细胞转移。④ 术后随访 12 个月,患者术后每 3~6 个月门诊复查,未复查者进行电话随访,记录患者的复发及相关并发症的情况。

1.4 统计学方法

采用 SPSS16.0 对数据进行统计学分析,计数资料以率(%)表示,组间比较行卡方检验,计量资料以($\bar{x}\pm s$)表示,组间比较行 t 检验,以 P<0.05 为差异有统计学意义。

2 结果

2.1 两组术中相关指标的比较

两组前哨淋巴结切除时间、术中出血量、淋巴结切除数量和主动脉旁淋巴结切除例数比较均无统计学差异(P>0.05),见表 1。

表 1 两组患者的术中相关指标的比较

Table 1 Comparison of the intraoperative related indicators between two groups

Groups	Case	SLN resection time (min)	Intraoperative blood loss	Number of lymph node dissection	Number of aortic lymph node resection
Control group	46	31.25± 8.74	95.32± 25.14	27.32± 7.25	20(43.48)
Observation group	47	33.01± 9.37	92.85± 23.64	28.36± 8.12	23(48.94)
x^2/t	-	-0.936	0.488	-0.651	0.279
P	-	0.352	0.627	0.517	0.598

2.2 两组的前哨淋巴结识别成功率的比较

观察组的前哨淋巴结识别成功率显著高于对照组 (P< 0.05),见表 2。

2.3 两种检查方法的准确率、敏感度和特异性比较

观察组患者的准确率和特异性均显著高于对照组 (P< 0.05),两组敏感度比较无统计学差异(P>0.05),见表 3。

2.4 两组患者的术后复发情况及并发症发生情况的比较

对照组患者的术后随访期间发现局部复发 3 例, 观察组无复发病例,两组复发率比较无统计学差异(P=0.361)。两组在随访期间均未发生皮肤坏死、过敏或永久性着色等相关不良反应。

3 讨论

前哨淋巴结是原发肿瘤淋巴结引流中最早累及的淋巴结,可反映其后整个区域淋巴结的受累情况,通过判断前哨淋巴结是否被肿瘤侵犯可对其后淋巴结是否转移进行评估,如前哨淋巴结阴性则其盆腹腔淋巴结未发生转移,无需进行系统性淋巴结清扫术,降低了并发症的发生和手术创伤[18-20]。前哨淋巴结的

表 2 两组的前哨淋巴结识别成功率的比较

Table 2 Comparison of the success rate of SLN identification between two groups

Groups	Case	Success	Failure	Success rate
Control group	46	39	7	84.78
Observation group	47	46	1	97.87
t	-			5.066
P	-			0.030

表 3 两种检查方法的准确率、敏感度和特异性比较[例(%)]

Table 3 Comparison of accuracy, sensitivity and specificity between two groups[n(%)]

Groups	Case	Accuracy	Sensitivity	Specificity
Control group	46	29/46(63.04)	46/46(100.00)	25/46(54.35)
Observation group	47	39/47(82.98)	47/47(100.00)	35/46(74.45)
t	-	4.700	-	4.111
P	-	0.030	-	0.043

识别已广泛应用于乳腺癌、阴道癌等肿瘤切除术，但在子宫内膜癌中的应用还比较少。示踪定位法是检测和识别前哨淋巴结的重要方式，目前分为染色法、核素法、染料核素结合法等，临床应用比较广泛的生物染料为亚甲蓝，但其检出率较低，且选择皮肤切口较盲目。同位素法有放射性，且设备昂贵，限制了其在临床的广泛应用[21-23]。近年来，随着医疗技术的不断发展，越来越多的染色材料应用于临床，吲哚菁绿可在近红外线下显示荧光，最初应用于肝脏疾病的诊断，目前已应用于乳腺癌的前哨淋巴结定位[24,25]。

为了寻求更有效的子宫内膜癌前哨淋巴结识别方法，本研究主要分析了吲哚菁绿联合亚甲蓝在子宫内膜癌患者前哨淋巴结识别中的应用效果。本研究结果显示吲哚菁绿联合亚甲蓝不影响患者的手术相关指标。亚甲蓝是一种最常见的前哨淋巴结示踪剂，可在氧化性环境中呈现蓝色。但其识别前哨淋巴结的精确性较低，假阳性和假阴性的发生率均较高，因此，单一的亚甲蓝染色不能满足临床的需求[26,27]。吲哚菁绿是一种水溶性的近红外免疫荧光染料，半衰期较短，主要通过肝脏代谢。有研究显示吲哚菁绿联合亚甲蓝在乳腺癌中前哨淋巴结的检出率明显高于单用亚甲蓝[28,29]。但吲哚菁绿在子宫内膜癌中的应用仍在起步阶段。本研究结果显示观察组的前哨淋巴结识别成功率、准确率和特异性显著高于对照组，说明吲哚菁绿联合亚甲蓝对子宫内膜癌患者前哨淋巴结的识别价值更高，在腹腔镜子宫内膜癌手术中具有较高的应用价值。该项技术在腹腔镜下能够直视肿瘤，可以精准的在肿瘤周围注射示踪剂，但该较为复杂，学习曲线较长，掌握难度较大，临床需系统的质量控制[30,31]。本研究随访 12 个月，两组患者的复发率无显著差异，且未发现明显的并发症，提示吲哚菁绿联合亚甲蓝应用于术中子宫内膜癌前哨淋巴结的识别不增加患者的复发率，且没有明显并发症，安全性较高。

综上所述，吲哚菁绿联合亚甲蓝在子宫内膜癌术中识别前哨淋巴结的应用价值显著高于单用亚甲蓝。

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