

本文引用:赵锦丽,刘光新,于鹤.不同部位注射咪喹鲁绿示踪下肢淋巴回流通路及子宫旁淋巴回流通路观察[J].新乡医学院学报,2024,41(3):262-265. DOI:10.7683/xyxyxb.2024.03.012.

【临床研究】

不同部位注射吲哚菁绿示踪下肢淋巴回流通路及子宫旁淋巴回流通路观察

赵锦丽, 刘光新, 于 鹤

(周口市中心医院妇科,河南 周口 466000)

摘要： **目的** 通过趾间注射与宫颈注射吡哆青绿示踪,观察下肢淋巴回流通路和子宫旁淋巴回流通路的不同之处。**方法** 选择2019年6月至2022年11月于周口市中心医院就诊的早期子宫内膜癌或宫颈癌患者50例为研究对象。根据术中吡哆青绿注射的部位将患者分为趾间注射组($n=20$)和宫颈注射组($n=30$)。2组患者分别在趾间及宫颈注射吡哆青绿,在荧光腹腔镜下观察下肢淋巴回流在盆腔内的通路以及子宫旁淋巴回流通路,重点观察二者的不同之处。**结果** 趾间注射组患者(20例40侧)中下肢淋巴回流在盆腔段显影18例(33侧),2例双侧未显影。显影的患者中有26侧显示下肢淋巴回流经腹股沟深淋巴结、旋髂淋巴结、髂外淋巴结、髂总淋巴结,5侧显示下肢淋巴回流至腹股沟深淋巴结、旋髂淋巴结、闭孔淋巴结、髂内淋巴结、髂总淋巴结,2侧显示下肢淋巴回流至腹股沟深淋巴结、闭孔淋巴结、髂内淋巴结、髂总淋巴结。宫颈注射组患者(30例60侧)中盆腔内淋巴显影29例55侧,1例双侧未显影。显影的患者中2侧显示宫旁淋巴回流至闭孔淋巴结、旋髂淋巴结、髂外淋巴结、髂总淋巴结,其中旋髂淋巴结均为非前哨淋巴结;40侧显示宫旁淋巴回流沿着上宫颈旁淋巴回流通路至髂外内侧淋巴结(或闭孔淋巴结)、髂总淋巴结;13侧显示沿着下宫颈旁淋巴回流通路至髂内淋巴结或骶前淋巴结。下肢淋巴回流与子宫旁淋巴回流的共同引流途径是由闭孔、髂外、髂总淋巴向上回流。趾间注射组和宫颈注射组旋髂淋巴结显影率分别为93.94%(31/33)、3.63%(2/55),趾间注射组旋髂淋巴结显影率显著高于宫颈注射组($P<0.05$)。**结论** 应用吡哆青绿示踪剂在荧光腹腔镜下能更直观地看到下肢淋巴回流及子宫旁淋巴回流通路,二者的淋巴回流不同之处在于下肢淋巴回流经髂外淋巴结远端的旋髂淋巴结,而宫颈癌和子宫内膜癌很少转移至此。

关键词: 吲哚菁绿;淋巴回流通路;下肢淋巴水肿;荧光腹腔镜

中图分类号: R737.3 文献标志码: A 文章编号: 1004-7239(2024)03-0262-04

Observations of lower limb lymphatic reflux and para-uterine lymphatic reflux by injecting indocyanine green

ZHAO Jinli, LIU Guangxin, YU He

(Department of Gynecology, Zhoukou Central Hospital, Zhoukou 466000, Henan Province, China)

Abstract: Objective To observe the differences between the lymphatic reflux in the lower extremities and near the uterus by interphalangeal and cervical injection of indocyanine green (ICG). **Methods** A total of 50 patients with early-stage endometrial cancer or cervical cancer admitted to Zhoukou Central Hospital from June 2019 to November 2022 were selected as the research subjects. According to the ICG injection site during the surgery, patients were divided into the interphalangeal injection group ($n=20$) and the cervical injection group ($n=30$). The patients in the two groups were injected with ICG at the toes or cervix uteri, respectively. The lower limb lymphatic reflux pathway in the pelvic cavity and the para-uterine lymphatic reflux pathway were observed under fluorescence laparoscopy, and the differences between the two groups were analyzed. **Results** Among the patients with the interphalangeal injection of ICG (20 patients, 40 sides), the lower limb lymphatic reflux was developed on 33 sides of 18 patients but not developed on both sides of 2 patients. Among the 18 patients, 26 sides showed the lower limb lymphatic reflux through deep inguinal lymph nodes, circumflex iliac lymph nodes, external iliac lymph nodes, and common iliac lymph nodes; 5 sides showed the lower limb lymphatic reflux to deep inguinal lymph nodes, circumflex iliac lymph nodes, obturator lymph nodes, internal iliac lymph nodes, and common iliac lymph nodes; and 2 sides showed the lower limb lymphatic reflux to deep inguinal lymph nodes, obturator lymph nodes, internal iliac lymph nodes, and common iliac lymph nodes. Among the patients with the cervical injection of ICG (30 patients, 60 sides), pelvic lymph nodes were developed on

DOI:10.7683/xxvxxxb.2024.03.012

收稿日期:2023-03-18

作者简介:赵锦丽(1984-),女,河南周口人,硕士,副主任医师,主要从事妇科疾病临床研究。

通信作者:刘光新(1968-),男,河南周口人,学士,主任医师,主要从事妇科疾病临床研究;E-mail:zklgx1968@sina.com

55 sides of 29 patients but not developed bilaterally in 1 patient. In the 29 patients, 2 sides showed para-uterine lymphatic reflux to obturator lymph nodes, circumflex iliac lymph nodes, external iliac lymph nodes, and common iliac lymph nodes, in which circumflex iliac lymph nodes were non-sentinel lymph nodes; 40 sides showed para-uterine lymphatic reflux to medial iliac lymph nodes (or obturator lymph nodes) and common iliac lymph nodes along the superior paracervical lymphatic reflux pathway; and 13 sides showed para-uterine lymphatic reflux to the internal iliac or presacral lymph nodes along the inferior paracervical lymphatic reflux pathway. The shared pathway of lower limb lymphatic reflux and para-uterine lymphatic reflux was upward reflux from obturator, external iliac and common iliac lymph nodes. The circumflex iliac lymph node developing rates in the interphalangeal and cervical injection groups were 93.94% (31/33) and 3.63% (2/55), respectively. The interphalangeal injection group had a significantly higher circumflex iliac lymph node developing rate than the cervical injection group ($P < 0.05$). **Conclusion** The application of ICG under fluorescence laparoscopy intuitively observed the lower limb lymphatic reflux and the para-uterine lymphatic reflux pathway. The difference between the two is that the lower limb lymphatic reflux flows through the circumflex iliac lymph nodes at the distal end of the external iliac lymph nodes, while cervical cancer and endometrial cancer rarely transfer there.

Key words: indocyanine green; lymphatic circulation pathway; lower limb lymphedema; fluorescence laparoscopy

下肢淋巴水肿是妇科恶性肿瘤手术后常见的并发症之一,其发生率为 20.0% ~ 67.4%^[1-4]。妇科恶性肿瘤手术清扫盆腔淋巴结导致的下肢淋巴水肿是由下肢淋巴回流障碍引起的,可导致下肢疼痛、肿胀等不适,重者影响患者的生活质量。妇科最常见的恶性肿瘤是宫颈癌和子宫内膜癌,这二者手术中均需进行盆腔淋巴结清扫术,如果能直观观察下肢淋巴回流至盆腔后的通路,将有助于术中避开或部分避开下肢淋巴回流通路以减少下肢水肿的发生。淋巴回流通路通常需要示踪剂来显示,既往应用的示踪剂有放射性核素⁹⁹Tc^m(放射性伤害)、亚甲蓝(显影效果差)等,因其各自的缺点均未在临床得到广泛应用。近年来临床广泛应用吲哚菁绿作为示踪剂,其优点是显影快、影像清晰、无毒副作用,但需要特殊的设备荧光腹腔镜。本研究应用吲哚菁绿分别示踪下肢淋巴回流通路及子宫内膜癌和宫颈癌的子宫旁淋巴回流通路,以期在荧光腹腔镜下更直观地观察子宫旁的淋巴回流与下肢的淋巴回流通路在盆腔内的不同之处,现将结果报道如下。

1 资料与方法

1.1 一般资料

选择 2019 年 6 月至 2022 年 11 月于周口市中心医院就诊的早期子宫内膜癌或宫颈癌患者 50 例为研究对象。病例纳入标准:(1)患者临床症状和体征符合子宫内膜癌 I 期、宫颈癌 I A、I B1 期的诊断标准;(2)患者术前经诊断性刮宫病理检查明确诊断为子宫内膜癌,经宫颈活检病理检查明确诊断为宫颈癌;(3)患者了解本次研究内容,并签署知情同意书;(4)既往无下肢手术病史者;(5)术前检查均无下肢瘢痕,无下肢水肿,无下肢静脉曲张,经下肢血管超声检查除外血管病变者;(6)患者术前

未接受放射治疗、化学治疗。排除标准:(1)对碘或吲哚菁绿等试剂过敏者;(2)无法耐受腹腔镜下子宫切除术或中转开腹者;(3)合并其他恶性肿瘤者;(4)合并其他系统严重疾病者。所有患者行腹腔镜盆腔淋巴结清扫术,根据术中吲哚菁绿注射的部位将患者分为趾间注射组($n = 20$)和宫颈注射组($n = 30$)。趾间注射组:年龄 43 ~ 55 (50.60 ± 3.31)岁;体质指数(body mass index, BMI)21 ~ 26 (24.05 ± 1.47) $\text{kg} \cdot \text{m}^{-2}$;盆腔淋巴结切除数 15 ~ 27 (20.60 ± 4.59)个;依据国际妇产科联盟(Federation International of Gynecology and Obstetrics, FIGO)分期标准^[5]对宫颈癌及子宫内膜癌进行分期,其中宫颈癌 9 例,FIGO 分期 I A 期 5 例, I B1 期 4 例;子宫内膜癌 I 期 11 例。宫颈注射组:年龄 36 ~ 56 (50.67 ± 4.55)岁; BMI 21 ~ 26 (24.00 ± 1.53) $\text{kg} \cdot \text{m}^{-2}$;宫颈癌 17 例,其中 FIGO 分期 I A 期 9 例, I B1 期 8 例;子宫内膜癌 I 期 13 例。2 组患者一般资料比较差异无统计学意义($P > 0.05$),具有可比性。本研究通过医院医学伦理委员会审核批准,所有患者签署知情同意书。

1.2 手术方法

患者取膀胱截石位,静脉吸入复合麻醉成功后,于脐孔上方约 2 cm 处做一长 1 cm 切口,建立 CO₂ 气腹,置入荧光腹腔镜,压力为 11 ~ 13 mm Hg (1 mm Hg = 0.133 kPa),头低臀高 30° ~ 45°。全面探查盆、腹腔内脏器及腹膜情况。

趾间注射组于患者双足第 1、2 及 4、5 趾间皮下缓慢注射 2.5 g · L⁻¹ 吲哚菁绿稀释液,每侧注射 1 mL,注射后 20 ~ 30 min 腹腔镜下观察盆腔淋巴显影情况。宫颈注射组于患者宫颈 3 点、9 点处浅层(1 ~ 3 mm)及深层(1 ~ 2 cm)缓慢注射 2.5 g · L⁻¹

吡啶菁绿稀释液 1 mL,注射点需距原发肿瘤病灶边缘 0.5 cm 以上,避免药物泄露。注射后 5 ~ 10 min 腹腔镜下观察盆腔淋巴显影情况。2 组患者均由至少 2 名妇科高级职称医师共同观察盆腔内淋巴结最先显影的部位,以及淋巴回流通路。

趾间注射组行系统性盆腔淋巴结清扫术,宫颈注射组先行前哨淋巴结活检后行系统性盆腔淋巴结清扫术。术后将切除的组织标本一起送病理检查。

1.3 统计学处理

应用 SPSS 22.0 软件对数据进行统计学分析。计量资料以均数 \pm 标准差 ($\bar{x} \pm s$) 表示,组间比较采用独立样本 t 检验;计数资料以例数和百分率表示,组间比较采用四格表 χ^2 检验或 Fisher 精确检验; $P < 0.05$ 为差异有统计学意义。

2 结果

趾间注射组患者(20 例 40 侧)中下肢淋巴回流在盆腔段显影 18 例(33 侧)(其中 3 例一侧显影),2 例双侧未显影。显影的患者中有 31 侧显示下肢淋巴回流经腹股沟深淋巴结、旋髂淋巴结,后进入髂内或髂外淋巴结、髂总淋巴结,2 侧显示下肢淋巴回流至腹股沟深淋巴结、闭孔淋巴结、髂内淋巴结、髂总淋巴结。

宫颈注射组患者(30 例 60 侧)中盆腔内淋巴显影 29 例 55 侧(其中 3 例一侧显影),1 例双侧未显影。显影的患者中 2 侧显示宫旁淋巴回流至闭孔淋巴结、旋髂淋巴结、髂外淋巴结、髂总淋巴结,其中旋髂淋巴结均为非前哨淋巴结;53 侧显示宫旁淋巴回流分别沿着上宫颈旁淋巴回流通路和下宫颈旁淋巴回流通路至髂总淋巴结。

下肢淋巴回流与子宫旁淋巴回流的共同引流途径:由闭孔、髂外、髂总淋巴向上回流。

趾间注射组和宫颈注射组髂外淋巴结远端的旋髂淋巴结显影率分别为 93.94% (31/33)、3.63% (2/55);趾间注射组髂外淋巴结远端的旋髂淋巴结显影率显著高于宫颈注射组,差异有统计学意义 ($P < 0.05$)。

3 讨论

手术是治疗妇科恶性肿瘤最主要方法之一,盆腔淋巴结清扫是手术的重要组成部分,术后淋巴回流障碍可出现淋巴囊肿或淋巴水肿,是目前妇科恶性肿瘤手术后最常见的并发症之一。文献报道,妇科恶性肿瘤手术后淋巴水肿发生率为 20.0% ~ 67.4%^[14],而临床上淋巴囊肿发生率为 1% ~

49%,个别文献报道术后 3 周淋巴囊肿发生率高达 88%^[1]。淋巴回流障碍所引起的淋巴囊肿或淋巴水肿不仅会引起患者疼痛、体质量增加及睡眠困难等不适感,甚至会增加患者病死率和罕见并发症的发生率。同时,由于下肢淋巴水肿会引起下肢肿胀,患者自尊心和自我形象等受到影响,严重影响了患者的身心健康和生活质量^[6-10]。此外,随着肿瘤治疗方式的完善及放化疗等辅助治疗技术的提高,患者的生存率有了一定程度的改善,此时更应着眼于提高患者的术后生存质量。本研究通过分析下肢和子宫旁淋巴回流通路的不同,可以指导妇科恶性肿瘤手术中避开下肢淋巴回流通路,能减少下肢淋巴水肿的发生,从而提高患者的生存质量

妇科恶性肿瘤患者由于行根治性手术及放射治疗,常导致淋巴管狭窄、闭塞及纤维化,当淋巴系统不能维持自身的稳态时,下腹部或下肢的皮肤或皮下组织常形成富含蛋白质的液体滞留,出现淋巴水肿^[11-13]。近年大量研究表明,保留髂外淋巴结远端的旋髂淋巴结(circumflex iliac nodes distal to the external iliac nodes, CINDEIN)可降低下肢淋巴水肿的发生率^[14-15]。

CINDEIN 是引流下肢的腹股沟深淋巴结或 Cloquet 淋巴结的直接延伸,其位于旋髂深静脉的远端。切除 CINDEIN 可能会增加术后下肢水肿的发生风险。多数文献报道,其他部位不存在淋巴结转移的宫颈癌和子宫内膜癌患者中,不会发生 CINDEIN 转移^[2,14,16-18]。YAMAZAKI 等^[14] 回顾性分析了 398 例行宫颈癌淋巴结切除术患者的临床资料,其中 199 例行切除 CINDEIN 的宫颈癌根治术,199 例行保留 CINDEIN 的宫颈癌根治术,结果发现,行切除 CINDEIN 的宫颈癌根治术患者术后出现下肢淋巴水肿的发生率显著高于行保留 CINDEIN 的宫颈癌根治术患者。有研究发现,清扫 CINDEIN 的宫颈癌患者下肢淋巴水肿发生率显著高于保留 CINDEIN 的患者^[17-18]。另外,TAKESHITA 等^[19] 对 531 例患者行宫颈癌根治性手术及盆腔淋巴结清扫术,结果发现,仅有 1.9% 的患者发生 CINDEIN 转移。说明宫颈癌中 CINDEIN 淋巴结转移率并不高。研究表明,CINDEIN 很少被认为是宫颈癌的前哨淋巴结,115 例存在前哨淋巴结转移患者中,1 例(0.9%)检测到 CINDEIN 为前哨淋巴结^[19]。本研究通过注射吡啶菁绿,直观地观察到子宫旁淋巴回流通路,其中髂外淋巴结远端的旋髂淋巴结显影率为 3.63%,与上述研究相符,说明切除髂外淋巴结远端的旋髂淋巴结对于子宫内膜癌和宫颈癌的治疗意义不大;而

在下肢淋巴回流通路中,髂外淋巴结远端的旋髂淋巴结显影率为 93.94%,表明髂外淋巴结远端的旋髂淋巴结是下肢淋巴回流通路中的重要环节。

本研究应用吲哚菁绿分别在趾间和宫颈注射,在荧光腹腔镜下观察下肢淋巴回流在盆腔内的通路以及子宫内膜癌和宫颈癌盆腔内的淋巴回流影像,并找到了下肢淋巴回流和子宫旁淋巴回流的共同引流途径:由闭孔、髂外、髂总淋巴向上回流。而下肢淋巴回流和子宫旁的淋巴回流通路不同的是下肢淋巴回流经髂外淋巴结远端的旋髂淋巴结,而子宫癌很少转移至此。因此在行子宫内膜癌和宫颈癌的盆腔淋巴清扫术中,避开旋髂淋巴结而进行其他的盆腔淋巴结的清扫,有助于减少对术后下肢淋巴回流的影响。

4 结论

本研究通过分别在趾间及宫颈注射吲哚菁绿,在荧光腹腔镜下观察下肢淋巴回流和子宫旁淋巴回流通路的不同,更直观地观察子宫旁的淋巴回流与下肢的淋巴回流通路在盆腔内的不同之处。下肢淋巴回流经髂外淋巴结远端的旋髂淋巴结,而子宫内膜癌和宫颈癌很少转移至此,故可以在以后的子宫内膜癌和宫颈癌患者中避开旋髂淋巴结进行盆腔淋巴结的清扫以减少下肢淋巴水肿的发生。

参考文献:

[1] KONDO E,TABATA T,SHIOZAKI T, *et al.* Large or persistent lymphocyst increases the risk of lymphedema, lymphangitis, and deep vein thrombosis after retroperitoneal lymphadenectomy for gynecologic malignancy[J]. *Arch Gynecol Obstet*,2013,288(3):587-593.

[2] TODO Y,YAMAMOTO R,MINOBE S, *et al.* Risk factors for postoperative lower-extremity lymphedema in endometrial cancer survivors who had treatment including lymphadenectomy[J]. *Gynecol Oncol*,2010,119(1):60-64.

[3] ARMBRUST R,AULETTA V,CICHON G, *et al.* Lymphedema after pelvic and para-aortic lymphadenectomy-results of a systematic evaluation in patients with cervical and endometrial carcinoma[J]. *Arch Gynecol Obstet*,2023,307(5):1557-1565.

[4] HAREYAMA H,HADA K,GOTO K, *et al.* Prevalence, classification, and risk factors for postoperative lower extremity lymphedema in women with gynecologic malignancies;a retrospective study[J]. *Int J Gynecol Cancer*,2015,25(4):751-757.

[5] KOH W J,ABU-RUSTUM N R,BEAN S, *et al.* Cervical cancer, version 3. 2019,NCCN clinical practice guidelines in oncology[J]. *J Natl Compr Canc Netw*,2019,17(1):64-84.

[6] ROWLANDS I J,BEESLEY V L,JANDA M, *et al.* Quality of life of women with lower limb swelling or lymphedema 3-5years following

endometrial cancer[J]. *Gynecol Oncol*,2014,133(2):314-318.

[7] SAHBAZ A,GUNGORDUK K,GULSEREN V, *et al.* What are the risk factors for lymphocyst formation apart from lymphnode dissection and lymphnode count in gynecologic malignancy[J]. *Geburtshilfe Frauenheilkd*,2016,76(4):403-407.

[8] CHEVILLE A L,ALMOZA M,COURMIER J N, *et al.* A prospective cohort study defining utilities using time trade-offs and the Euroqol-5D to assess the impact of cancer-related lymphedema[J]. *Cancer*,2010,116(15):3722-3731.

[9] WEDIN M,STÅLBERG K,MARCICKIEWICZ J, *et al.* Impact of lymphadenectomy and lymphoedema on health-related quality of life 1 year after surgery for endometrial cancer. A prospective longitudinal multicentre study[J]. *BJOG*,2022,129(3):450-460.

[10] CARTER J,HUANG H Q,ARMER J, *et al.* GOG 244-The Lymphedema and Gynecologic cancer (LeG) study;the impact of lower-extremity lymphedema on quality of life,psychological adjustment, physical disability, and function[J]. *Gynecol Oncol*,2021,160(1):244-251.

[11] KI E Y,PARK J S,LEE K H, *et al.* Incidence and risk factors of lower extremity lymphedema after yncologic surgery in ovarian cancer[J]. *Int J Gynecol Cancer*,2016,26(7):1327-1332

[12] BRIX B,SERY O,ONORATO A, *et al.* Biology of Lymphedema[J]. *Biology (Basel)*,2021,10(4):261.

[13] DUHON B H,PHAN T T,TAYLOR S L, *et al.* Current mechanistic understandings of lymphedema and lipedema; tales of fluid, fat, and fibrosis[J]. *Int J Mol Sci*,2022,23(12):6621.

[14] YAMAZAKI H,TODO Y,TAKESHITA S, *et al.* Relationship between removal of circumflex iliac nodes distal to the external iliac nodes and postoperative lower-extremity lymphedema in uterine cervical cancer[J]. *Gynecol Oncol*,2015,139(2):295-299.

[15] TOGAMI S,KUBO R,KAWAMURA T, *et al.* Risk factors for lymphatic complications following lymphadenectomy in patients with endometrial cancer[J]. *Taiwan J Obstet Gynecol*,2020,59(3):420-424.

[16] OHBA Y,TODO Y,KOBAYASHI N, *et al.* Risk factors for lower-limb lymphedema after surgery for cervical cancer[J]. *Int J Clin Oncol*,2011,16(3):238-243.

[17] TODO Y,YAMAZAKI H,TAKESHITA S, *et al.* Close relationship between removal of circumflex iliac nodes to distal external iliac nodes and postoperative lower-extremity lymphedema in uterine corpus malignant tumors[J]. *Gynecol Oncol*,2015,139(1):160-164

[18] VIVEROS-CARREÑO D,RODRIGUEZ J,PAREJA R. Incidence of metastasis in circumflex iliac nodes in patients with cervical cancer;a systematic review[J]. *Int J Gynecol Cancer*,2021,31(12):1530-1534.

[19] TAKESHITA S,TODO Y,OKAMOTO K, *et al.* Incidence of metastasis in circumflex iliac nodes distal to the external iliac nodes in cervical cancer[J]. *J Gynecol Oncol*,2016,27(4):e42.