

阑尾切除术在卵巢上皮性肿瘤中的应用探讨

王 喆, 张 颐

(中国医科大学附属第一医院, 辽宁 沈阳 110001)

摘要: 阑尾不仅具有免疫功能, 而且能够调节肠道菌群平衡, 在维持机体稳态中起重要作用。阑尾与卵巢肿瘤的转移密切相关。不同类型的卵巢上皮性肿瘤是否应切除阑尾, 一直备受争议。对于卵巢黏液性肿瘤, 应重点关注阑尾外观情况、是否伴有腹膜假黏液瘤等转移病灶。若上述指标无异常, 则不推荐行阑尾切除术。针对卵巢浆液性肿瘤, 目前观点尚有分歧, 有待进一步探索阑尾切除术在浆液性肿瘤中的最佳适应证。总之, 阑尾对人体具有保护作用, 切除阑尾并不能明显改善患者的预后, 同时存在潜在的并发症。无论是哪种类型的卵巢上皮性肿瘤, 均应尽量避免切除无病变的阑尾。

主题词: 良性卵巢囊腺瘤; 交界性卵巢肿瘤; 卵巢癌; 阑尾切除术

中图分类号: R713.6 **文献标识码:** A **文章编号:** 1671-170X(2021)11-0967-04

doi: 10.11735/j.issn.1671-170X.2021.11.B013

Options of Appendectomy in Surgical Treatment of Epithelial Ovarian Tumor

WANG Zhe, ZHANG Yi

(The First Hospital of China Medical University, Shenyang 110001, China)

Abstract: The human appendix not only plays an important role in improving immunity but also contributes to regulating the balance of intestinal flora. However, the appendix is also closely associated with the metastasis of ovarian tumor. Whether the appendix should be removed has been controversial in different types of epithelial ovarian tumor. For mucinous ovarian tumor, if the appearance of the appendix is normal and there is no sign of pseudomyxoma peritonei, the appendectomy is not recommended. As for ovarian serous ovarian tumor, there is still controversial for the most adaptable indication of appendectomy. To sum up, the appendix confers multiple protective effects on the human body, appendectomy does not seem to have a significant impact on the prognosis of patients with epithelial ovarian neoplasms, and the appendectomy has potential complications. Accordingly, we should avoid removing the appendix without definite indications in all types of epithelial ovarian tumor.

Subject words: benign ovarian cystadenoma; borderline ovarian tumor; ovarian cancer; appendectomy

现代医学认为, 阑尾不仅具有免疫保护功能, 而且能够维持肠道微生态平衡^[1]。阑尾能够分泌免疫球蛋白 A 等多种物质, 同时可将共生菌排入肠道, 为其补充健康的菌群^[2]。阑尾与卵巢肿瘤密切相关, 特别是卵巢黏液性肿瘤。多数黏液性肿瘤由胃肠道起源, 容易向卵巢、腹膜等部位转移^[3-4]。阑尾黏液性肿瘤可导致卵巢黏液性囊腺瘤、腹膜假黏液瘤(pseudomyxoma peritonei, PMP)等肿瘤发生。

2021 年 NCCN 卵巢癌临床实践指南提出, 黏液性卵巢癌需切除外观异常的阑尾^[5]。法国妇产科学

院最新指南建议, 对于卵巢交界性肿瘤, 仅在阑尾外观明显异常时才需要行阑尾切除术^[6]。但是, 对于阑尾外观“异常”的概念、浆液性卵巢肿瘤或伴有其他情况的卵巢肿瘤的阑尾处理方式, 指南中并未明确说明。此外, 阑尾切除术存在出血、腹膜炎、腹腔内脓肿、肠穿孔等潜在并发症, 使术后感染风险增高^[7-8]。因此, 有必要探讨阑尾切除术在不同类型卵巢上皮性肿瘤中的适用情况, 以更好地指导临床实践。

1 黏液性肿瘤

1.1 良性卵巢黏液性囊腺瘤

良性卵巢黏液性囊腺瘤患者的阑尾同时病变的

基金项目: 国家重点研发计划项目资助(2018YFC1311600); 辽宁省中央引导地方科技发展专项(2019JH6/10400006)

通信作者: 张颐, 科主任, 主任医师, 教授, 博士研究生导师, 博士; 中国医科大学附属第一医院妇科, 辽宁省沈阳市和平区南京北街 155 号(110001); E-mail: syzi@163.com

收稿日期: 2021-05-06; **修回日期:** 2021-06-18

概率较低,只有当阑尾外观出现管壁增厚、充血、粘连等异常,或者病理诊断为阑尾黏液囊肿、阑尾炎及阑尾类癌等情况时,才推荐行阑尾切除术^[9-10]。Timofeev等^[10]研究发现,59例阑尾外观正常的良性卵巢黏液性囊腺瘤中,仅发现1例阑尾病理异常。在12例阑尾出现纤维化、充血、粘连等情况时,却发现4例阑尾同时存在炎症、类癌等病理异常。Ozyurek等^[11]认为,对于阑尾形态正常的卵巢黏液性囊腺瘤,不必行阑尾切除术。然而,部分学者认为卵巢黏液性囊腺瘤常继发于阑尾黏液性肿瘤,两者关系密切。Shaib等^[12]发现,阑尾黏液性肿瘤经常向卵巢和腹膜转移。卵巢黏液性囊腺瘤和阑尾黏液性肿瘤可能具有同源性。有学者建议常规探查患者阑尾,必要时可行阑尾切除术。

PMP与卵巢黏液性肿瘤可能有关,虽然PMP大多起源于阑尾假黏液瘤,但少数也可来自卵巢黏液性囊腺瘤^[13-14]。对于伴有PMP的卵巢黏液性囊腺瘤,有必要判断PMP的来源。若PMP来自阑尾转移,那么有必要实施阑尾切除术,若PMP起自卵巢黏液性囊腺瘤,在切除卵巢肿瘤的同时,是否有必要切除阑尾还有待商榷。

1.2 卵巢黏液性交界性肿瘤

对于卵巢黏液性交界性肿瘤(mucinous borderline ovarian tumor, mBOT)是否有必要切除阑尾?部分学者认为,由于实施阑尾切除术可排除阑尾原发性或转移性肿瘤,并指导肿瘤分期,同时可作为肿瘤细胞减灭术的一部分,支持切除mBOT患者的阑尾^[15-17]。然而,mBOT发生阑尾原发性或转移性肿瘤的概率很低。数据显示,mBOT阑尾浸润性转移的发生率约0.86%,正常外观的阑尾发生转移的概率则更低^[17]。另外,切除阑尾并不能改善患者的生存期。Gungorduk等^[18]对364例mBOT预后相关因素分析发现,无论阑尾切除与否,总体生存期和肿瘤复发率均无统计学差异。阑尾切除术不仅具有潜在的并发症,而且对患者预后无益。因此,应尽量避免切除无病变的阑尾。

寻找阑尾病变的预测指标成为了近年来的研究热点。最近,许多学者认为,阑尾外观可作为阑尾病变的潜在预测指标。对于阑尾外观异常的mBOT,建议行阑尾切除术。一项Meta分析报道^[19],在发生阑尾转移的mBOT中,阑尾外观同时存在增粗、包裹

成团、与周围粘连或粟粒样结节等改变。Ozcan等^[20]对22例外观严重异常的阑尾进行病理检查,结果发现阑尾淋巴组织增生、阑尾黏液囊肿和阑尾类癌等异常改变。阑尾外观无异常65例,其阑尾病理诊断均正常。Solmaz等^[21]认为,术中探查时要特别注意mBOT的阑尾外观情况,不推荐将正常外观的阑尾切除。

此外,当mBOT伴有PMP等转移病灶时,建议将阑尾同时切除并进行组织学检查。研究发现,约90% PMP是由阑尾假黏液瘤种植性转移而来,PMP患者常存在阑尾黏液性病变或阑尾切除史^[22-23]。Ramaswamy^[24]报道,PMP形成过程始于阑尾,阑尾杯状细胞先发生肿瘤化,形成阑尾黏液性肿瘤。随后向深部侵犯至阑尾壁,当阑尾发生微小穿孔或破裂时,就会以胶状沉积物的形式扩散入腹腔,导致PMP的发生。Di等^[25]也认为PMP大多由阑尾黏液性肿瘤继发种植转移而来。由于PMP和卵巢黏液性肿瘤关系密切,当mBOT患者伴有PMP时,应考虑将阑尾切除^[20]。

1.3 黏液性卵巢癌

2021年卵巢癌临床实践指南强调,无需常规切除黏液性癌患者的阑尾,只有在阑尾外观异常时才有必要将其切除^[5]。阑尾并非黏液性卵巢癌的最先转移部位,只有当阑尾壁增厚、质硬、呈结节性或囊性、局部淋巴结肿大时,才应考虑将阑尾切除^[26]。一项Meta分析显示,在发生阑尾转移的黏液性卵巢癌患者中,阑尾外观均出现增粗、粘连成团、表面粗糙等异常改变^[19]。此外,Elias等^[27]提出阑尾切除术无保护作用,即使切除阑尾也不会降低患病风险,患者不会因此获益。因此,手术过程中应仔细检查阑尾情况,若发现阑尾外观正常且无PMP等转移病灶时,不推荐行阑尾切除术。

2 浆液性肿瘤

2.1 良性卵巢浆液性囊腺瘤

与良性卵巢黏液性囊腺瘤相似,浆液性囊腺瘤出现阑尾受累的概率较低。Timofeev等^[10]指出,在35例浆液性囊腺瘤中,未发现阑尾存在病理异常。由于良性卵巢浆液性肿瘤出现阑尾病变的可能性不大,只有当阑尾出现管壁增厚、充血、粘连等异常情况时,才有必要切除阑尾。鉴于目前有关浆液性囊腺

瘤阑尾处理的报道有限, 还需更多的研究来提供理论依据。

2.2 卵巢交界性浆液性肿瘤

目前, 学者对卵巢交界性浆液性肿瘤 (serous borderline ovarian tumor, sBOT) 的阑尾病变情况仍有分歧。Timofeev 等^[10]认为 sBOT 的阑尾病变可能性较低, 在 12 例 sBOT 患者中仅发现 1 例存在阑尾病变。Guvenal 等^[28]对此意见相反, 他们对 539 例交界性卵巢肿瘤病例分析发现, 约 40% 患者接受了阑尾切除术, 其中大部分属于 sBOT。与 mBOT 相比, 阑尾切除术似乎更常用于 sBOT 患者。由于学者对 sBOT 阑尾病变情况还未达成共识, 是否可以参照 mBOT 切除阑尾的适用条件, 还需进一步探讨。

2.3 浆液性卵巢癌

浆液性卵巢癌发生阑尾转移的概率更高, 目前更倾向于行阑尾切除术。数据显示, 约 60% 浆液性卵巢癌会出现阑尾转移, 且绝大多数阑尾转移源自晚期肿瘤患者^[10]。一项对 90 例原发性卵巢癌研究发现, 其中 49 例浆液性癌出现阑尾转移, 而黏液性癌却无一例发生阑尾转移^[29]。多数学者一致表示, 与黏液性癌相比, 浆液性卵巢癌更易转移至阑尾^[30]。因此, 为了排除阑尾转移的可能, 建议对浆液性卵巢癌患者行阑尾切除术, 同时将其作为肿瘤细胞减灭术的一部分; 但是, 是否所有患者均有必要将阑尾切除尚无统一标准。

3 结 语

阑尾对人体具有重要的保护作用, 无论是哪种类型的卵巢上皮性肿瘤, 均应尽量避免切除无病变的阑尾。阑尾外观、伴有 PMP 等转移疾病以及冰冻切片病理诊断等, 可作为阑尾病变的重要预测指标。当阑尾出现管壁增厚、粘连、纤维化、结节、充血等改变时, 提示阑尾外观“异常”^[9-10, 20]。此外, 卵巢上皮性肿瘤的组织学类型、手术病理分期等也可能与阑尾病变有关。早期 (I~II 期) 患者阑尾受累的风险较低, 而晚期 (III~IV 期) 患者阑尾出现转移的可能性较高^[11, 21]。对于早期交界性卵巢肿瘤, 若阑尾大体无异常, 阑尾受累的比例常低于 3%。因此, 早期患者应仔细评估阑尾大体情况, 对待阑尾切除术应持谨慎态度^[31-32]。

阑尾原发性或转移性肿瘤的发生率较低, 切除阑尾会因潜在的并发症使手术时间延长而增加风险^[20, 31, 33]。当阑尾外观异常或伴有 PMP 等转移病灶时, 才推荐切除阑尾。对于良性卵巢上皮性肿瘤, 无论是黏液性还是浆液性囊腺瘤, 阑尾发生病变的概率均较低。如果阑尾外观未出现上述异常, 不建议将阑尾切除。mBOT 和黏液性卵巢癌对阑尾的处理类似, 支持对阑尾外观异常及伴有 PMP 等转移病灶的患者行阑尾切除术, 这一观点与最新的卵巢癌临床实践指南相一致^[5, 15]。对于 sBOT 和浆液性卵巢癌, 目前的文献报道有限。浆液性卵巢癌同时存在阑尾病变的可能性更大, 目前更倾向于对这部分患者行阑尾切除术^[7]。今后有待进一步研究阑尾切除术在浆液性卵巢肿瘤中的适用情况。

总之, 阑尾并非人类退化的无用器官, 在各种类型的卵巢上皮性肿瘤手术过程中, 不推荐将无病变的阑尾切除。因此, 在手术时应仔细检查阑尾, 尤其是阑尾外观及其病理检查是否异常, 同时要注意患者是否伴有 PMP 等转移性疾病, 对于阑尾切除术应谨慎对待。今后应进一步探讨阑尾切除术在卵巢上皮性肿瘤中的适应证, 以减少不必要的阑尾切除。同时, 还应加强对各种浆液性卵巢肿瘤的研究, 探讨阑尾受累的情况。

参考文献:

- [1] Sanchez-Alcoholado L, Fernandez-Garcia JC, Gutierrez-Repiso C, et al. Incidental prophylactic appendectomy is associated with a profound microbial dysbiosis in the long-term[J]. *Microorganisms*, 2020, 8(4): 609.
- [2] Girard-Madoux MJH, Gomez De Aguero M, Ganai-Vonarb SC, et al. The immunological functions of the appendix: an example of redundancy? [J]. *Semin Immunol*, 2018, 36: 31-44.
- [3] Li Z, Roth R, Rock JB, et al. Dual immunostain with SATB2 and CK20 differentiates appendiceal mucinous neoplasms from ovarian mucinous neoplasms[J]. *Am J Clin Pathol*, 2017, 147(5): 484-491.
- [4] Rosenblum RC, Klein N, Paran H, et al. Appendiceal tumor incidence and an in-depth look at appendiceal neuroendocrine neoplasm in a cohort of 8,162 appendectomies: full dataset[J]. *Data in brief*, 2020, 33: 106456.
- [5] 卢淮武, 许妙纯, 张钰豪, 等. 《2021 NCCN 卵巢癌包括输卵管癌及原发性腹膜癌临床实践指南 (第 1 版)》解读 [J]. *中国实用妇科与产科杂志*, 2021, 37(4): 457-466. Lu HW, Xu MC, Zhang YH, et al. Interpretation of 2021 NCCN guidelines to the clinical practice in ovary cancer including fallopian tubercancer and primary peritoneal can-

- cer (Version 1) [J]. Chinese Journal of Practical Gynecology and Obstetrics, 2021, 37(4): 457–466.
- [6] Canlorbe G, Lécointre L, Chauvet P, et al. Borderline ovarian tumours; CNGOF guidelines for clinical practice – therapeutic management of early stages [J]. Gynecol Obstet Fertil Senol, 2020, 48(3): 287–303.
- [7] Altman AD, Lefas G, Power L, et al. Rate of appendiceal metastasis with non-serous epithelial ovarian cancer in manitoba [J]. J Obstet Gynaecol Can, 2018, 40(2): 180–185.
- [8] Bernard L, Chen I, Le T. Appendectomy at the time of ovarian cancer staging increases infectious complications: a national surgical quality improvement program (NSQIP) propensity score-stratified analysis [J]. Int J Gynecol Cancer, 2020, 30(10): 1542–1547.
- [9] 陈敬. 阑尾黏液性肿瘤与卵巢黏液性囊腺瘤的临床病理分析 [J]. 实用妇科内分泌电子杂志, 2019, 6(24): 27.
Chen J. Clinicopathological analysis of appendiceal mucinous tumor and ovarian mucinous cystadenoma [J]. Electronic Journal of Practical Gynecologic Endocrinology, 2019, 6(24): 27.
- [10] Timofeev J, Galgano MT, Stoler MH, et al. Appendiceal pathology at the time of oophorectomy for ovarian neoplasms [J]. Obstet Gynecol, 2010, 116(6): 1348–1353.
- [11] Ozyurek ES, Karacaoglu UM, Kaya E, et al. Appendectomy in the surgical treatment of benign ovarian mucinous cystadenomas- is it necessary? [J]. Ginek Pol, 2016, 87(5): 338–341.
- [12] Shaib WL, Assi R, Shamseddine A, et al. Appendiceal mucinous neoplasms: diagnosis and management [J]. Oncologist, 2017, 22(9): 1107–1116.
- [13] Noguchi R, Yano H, Gohda Y, et al. Molecular profiles of high-grade and low-grade pseudomyxoma peritonei [J]. Cancer Med, 2015, 4(12): 1809–1816.
- [14] Yan F, Shi F, Li X, et al. Clinicopathological characteristics of pseudomyxoma peritonei originated from ovaries [J]. Cancer Manag Res, 2020, 12: 7569–7578.
- [15] Kleppe M, Bruls J, Van Gorp T, et al. Mucinous borderline tumours of the ovary and the appendix: a retrospective study and overview of the literature [J]. Gynecol Oncol, 2014, 133(2): 155–158.
- [16] Seong SJ, Kim DH, Kim MK, et al. Controversies in borderline ovarian tumors [J]. J Gynecol Oncol, 2015, 26(4): 343–349.
- [17] Cosyns S, De Sutter P, Tournaye H, et al. Necessity of appendectomy for mucinous borderline ovarian tumors. systematic review [J]. Arch Gynecol Obstet, 2016, 294(6): 1283–1289.
- [18] Gungorduk K, Asicioglu O, Braicu EI, et al. The impact of surgical staging on the prognosis of mucinous borderline tumors of the ovaries: a multicenter study [J]. Anticancer Res, 2017, 37(10): 5609–5616.
- [19] 程傲霜. 180 例卵巢黏液腺癌病例分析及阑尾切除 Meta 分析 [D]. 济南: 山东大学, 2017.
Cheng AS. Retrospective study of 180 malignant mucinous ovarian neoplasms and system meta-analysis about routine appendectomy [D]. Jinan: Shandong University, 2017.
- [20] Ozcan A, Toz E, Turan V, et al. Should we remove the normal-looking appendix during operations for borderline mucinous ovarian neoplasms? a retrospective study of 129 cases [J]. Int J Surg, 2015, 18: 99–103.
- [21] Solmaz Hasdemir P, Guvena T. Borderline ovarian tumors: a contemporary review of clinicopathological characteristics, diagnostic methods and therapeutic options [J]. J Buon, 2016, 21(4): 780–786.
- [22] Van Eden WJ, Kok NFM, Snaebjornsson P, et al. Factors influencing long-term survival after cytoreductive surgery and hyperthermic intraperitoneal chemotherapy for pseudomyxoma peritonei originating from appendiceal neoplasms [J]. BJS Open, 2019, 3(3): 376–386.
- [23] Ishida M, Mizumoto A, Yonemura Y, et al. Prognostic significance of the presence of epithelial cell clusters in the ascites of patients with pseudomyxoma peritonei [J]. Diagn Cytopathol, 2019, 47(10): 1024–1027.
- [24] Ramaswamy V. Pathology of mucinous appendiceal tumors and pseudomyxoma peritonei [J]. Indian J Surg Oncol, 2016, 7(2): 258–267.
- [25] Di Leo A, Corvasce A, Weindelmayer J, et al. Cytoreductive surgery (CRS) and hyperthermic intraperitoneal chemotherapy (HIPEC) in pseudomyxoma peritonei of appendiceal origin: result of a single centre study [J]. Updates Surg, 2020, 72(4): 1207–1212.
- [26] 刘映, 李代强. 阑尾恶性肿瘤 9 例临床病理分析 [J]. 实用医学杂志, 2007, 23(12): 1889–1890.
Liu Y, Li DQ. Clinicopathological analysis of 9 cases of appendiceal malignant tumor [J]. The Journal of Practical Medicine, 2007, 23(12): 1889–1890.
- [27] Elias KM, Labidi-Galy SI, Vitonis AF, et al. Prior appendectomy does not protect against subsequent development of malignant or borderline mucinous ovarian neoplasms [J]. Gynecol Oncol, 2014, 132(2): 328–333.
- [28] Guvenal T, Dursun P, Hasdemir PS, et al. Effect of surgical staging on 539 patients with borderline ovarian tumors: a Turkish gynecologic oncology group study [J]. Gynecol Oncol, 2013, 131(3): 546–550.
- [29] Bese T, Kosebay D, Kaleli S, et al. Appendectomy in the surgical staging of ovarian carcinoma [J]. Int J Gynaecol Obstet, 1996, 53(3): 249–252.
- [30] Lin JE, Seo S, Kushner DM, et al. The role of appendectomy for mucinous ovarian neoplasms [J]. Am J Obstet Gynecol, 2013, 208(1): 46e1–4.
- [31] Boyajian H, Majeski V, Flores A, et al. Clinicopathological and perioperative outcome of appendiceal tumors: case review of 31 patients [J]. Spartan Med Res J, 2020, 5(2): 13487.
- [32] Bourdel N, Huchon C, Abdel Wahab C, et al. Borderline ovarian tumors: French guidelines from the CNGOF. Part 2. Surgical management, follow-up, hormone replacement therapy, fertility management and preservation [J]. J Gynecol Obstet Hum Reprod, 2021, 50(1): 101966.
- [33] Song T, Kim MK, Jung YW, et al. The role of appendectomy in patients with mucinous borderline ovarian tumors [J]. Eur J Obstet Gynecol Reprod Biol, 2018, 229: 112–116.