

早期宫颈癌手术方式的研究进展

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摘要:早期宫颈癌手术方式主要包括开腹手术和腹腔镜手术, 由于缺乏一项满意的前瞻性随机对照研究来证明这两种手术方式之间的差异, 所以对于早期宫颈癌最佳手术方式的选择一直以来争议不断。近期发表的两项早期宫颈癌腹腔镜子宫切除术对比开腹子宫切除术的研究使大家对两种手术方式的选择有了重新认识, 开腹手术组的总生存率和无病生存率明显高于腹腔镜手术组, 而腹腔镜手术组的局部复发率和累积死亡率明显高于开腹手术组, 两者的术后并发症和 1 周后生活质量则无明显差异。因此开腹手术被认为是早期宫颈癌广泛子宫切除术的标准程序, 但并不能因此完全否定腹腔镜手术价值, 应该对腹腔镜手术中存在的问题加以改进。

关键词:宫颈癌; 腹腔镜; 开腹手术; 无病生存; 根治性子宫切除术

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Research Progress on Surgical Treatment of Early Cervical Cancer

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Abstract: Laparotomy and laparoscopy are two main surgical modalities for treatment of early cervical cancer. Due to lack of data from prospective randomized controlled trials, there has been controversy about the choice of surgical approaches for early cervical cancer. However, two recently published studies have brought new insight into the choice of laparoscopy or laparotomy for treatment of early cervical cancer. The overall survival rate and disease-free survival rate of the laparotomy group were significantly higher than those of the laparoscopy group. The local recurrence rate and cumulative mortality of the laparoscopy group were significantly higher than those of the laparotomy group. There were no significant differences in the postoperative complications and the quality of life after 1 week of the procedure between two approaches. Therefore, laparotomy is considered to be the standard procedure for extensive hysterectomy for early cervical cancer, but the advantages of laparoscopy should not be neglected and its related problems should be improved.

Subject words: cervical cancer; laparoscopy; laparotomy; disease-free survival; radical hysterectomy

1 宫颈癌手术发展史

1992 年第一例腹腔镜下宫颈癌根治术, 推动了微创技术在妇科恶性肿瘤治疗中的进展。早期宫颈癌患者多采用手术治疗为主, 放化疗为辅的综合性治疗方案; 而晚期的宫颈癌患者, 治疗主要以放疗为主, 化疗为辅^[1-2]。根据患者的治疗方案、自身免疫力等因素的不同, 复发率也存在一定的差异。对于可

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手术治疗的早期宫颈癌患者, 可以选择的手术方案有以下 3 种: (1) 开腹手术; (2) 腹腔镜手术; (3) 经阴道和腹腔镜联合手术^[3-5]。由于经阴道和腹腔镜联合手术优势并不显著, 所以逐渐被摒弃。现在早期宫颈癌患者的手术治疗, 主要采用开腹手术或腹腔镜手术。以往大多数学者认为与开腹手术相比, 腹腔镜下宫颈癌根治术存在许多优点: 如腹壁切口小且痛感轻微; 视野清晰出血少; 对肠道干扰少; 术后感染率低; 并发症相对开腹手术少; 术后生活质量提高; 复发率与死亡率与开腹手术相比无统计学差异等^[6-9]。因此, 临床医生越来越提倡腹腔镜下宫颈癌根治术,

同时该术式也被患者接受认可,近 20 年来在国内迅速发展。

2 宫颈癌手术方式新观点及研究成果

2.1 早期宫颈癌手术方式新观点

2018 年 11 月份,《新英格兰医学杂志》同时刊登了 2 篇改变宫颈癌手术方式的文章,文章提出对于早期宫颈癌患者的最佳手术治疗方式为开腹手术^[10-11]。2019 第 3 版 NCCN 指南指出开腹手术是早期宫颈癌广泛子宫切除术的标准程序^[12]。

2.2 宫颈癌不同手术方式带来不同的治疗结局

在 2019 年 3 月举行的美国妇科肿瘤学会(society of gynecologic oncology,SGO)会议上,发表在《新英格兰医学杂志》上的一项前瞻性多中心随机对照研究,针对腹腔镜下行广泛全子宫切除术与开腹行广泛全子宫切除术做了比较,在该研究中,将 631 例早期 I A1 淋巴管腔侵犯 (lymph-vascular space invasion, LVSI), I A2, I B1 的鳞癌、腺癌、腺鳞癌的患者随机分成两组,其中 312 例行开腹广泛全子宫切除术,319 例行腹腔镜或机器人辅助下广泛全子宫切除术,两组基线资料无统计学差异,包括年龄、体质指数 (body mass index,BMI)、分期、病灶体积、病理类型、组织分级、中高危因素、淋巴结切除数目、阴道切缘、术后辅助治疗等,结果显示:与开腹手术相比,微创组 4.5 年无病生存率 (disease free survival, DFS)为 86%,而开腹组为 96.5%;尤其是局部复发率(local recurrence rate,LRR),微创手术组明显高于开腹手术组;微创手术组的无进展生存期(progression-free-survival,PFS)差于开腹手术组;开腹组累积死亡率(disease specific survival)明显低于微创组(0.6% vs 4.4%),微创组比开腹组多 16 例死亡;总生存率(overall survival,OS)微创组显著性低于开腹组(93.8% vs 99.0%);34 例术后复发的患者,微创组占 27 例,开腹组占 7 例,大多数患者的复发病灶均发生于盆腔,而盆腔外有复发灶的病例均为微创组。这项研究表明,与开腹手术相比,微创行宫颈癌根治术与更低的无病生存率、总生存率有关^[10,13]。其他数据同样显示接受开腹根治性子宫切除术患者的 5 年无病生存率为 93.3%~94.4%,与上述前瞻性试验中开腹组 4.5 年无病生存率几乎一致^[14-16]。2019 年举行的美国临床肿瘤学会 (American society of clinical

oncology,ASCO)会议上一项口头报告回顾性分析指出,在 2010~2017 年多个中心接受根治性子宫切除的 I A1、I A2 和 I B1 期鳞癌、腺癌或腺鳞癌患者中,根据 185 例(26.3%)行宫颈癌根治术开腹手术和 519 例(73.7%)行腹腔镜手术患者的数据,在校正了种族、合并症、术前肿瘤大小、组织学类型、肿瘤分级后,微创手术组患者复发风险明显高于开腹手术组。

2018 年在芝加哥举办的美国临床肿瘤学会(ASCO)会议上,一项关于宫颈癌开腹手术与腹腔镜手术治疗的回顾性分析表明,根据 2010~2012 年美国国家癌症资料库(national cancer database,NCDB)中 1166 例(52.5%)行宫颈癌根治术开腹手术和 1055 例(47.5%)行腹腔镜手术患者的数据,两组之间基线资料和随访时间无统计学差异,腹腔镜手术后患者的死亡风险相比开腹手术增加了 48%,认为腔镜组与早期宫颈癌患者低生存率和高复发风险相关^[11]。

2018 年在日本举行的 IGCS (the International Gynecologic Cancer Society)会议上,有专家指出早期宫颈癌患者微创术后的并发症与开腹术后相比无统计学差异^[17]。另一篇会议发言指出早期宫颈癌患者微创术后的生活质量与开腹术后无统计学差异,其中仅有的细微差别在于开腹手术的患者由于术后腹部切口较大,术后 1 周的生活自理程度略差于微创患者,而 1 周后两组术后生活质量无统计学差异^[18]。所以无论是在术后并发症方面还是生活质量方面,微创手术的优势将不复存在。

综上,我们认为:(1)早期宫颈癌患者微创术后复发率比开腹手术高 4 倍;(2)早期宫颈癌患者微创术后死亡率比开腹手术高 6 倍;(3)两组手术术后并发症、1 周后生活质量无统计学差异;(4)术后短期和长期生存率两组无统计学差异^[10,13-18]。

3 宫颈癌手术方式利弊的探讨

3.1 宫颈癌腹腔镜手术中存在的问题及改善方式

我们既不能全盘否定腔镜技术,也不能完全无视研究结果。我们必须寻找可能原因加以改进,需开展更多前瞻性随机对照研究。微创手术中存在的主要问题为:(1)举宫器(包括举宫杯和螺旋形子宫托)^[19-20];(2)肿瘤污染腹腔;(3)CO₂气腹;(4)学习

曲线; (5) 切除范围不够^[9, 21-23]等。2019 年 ASCO 会议上一项口头回顾性分析显示, 26 例微创手术中未使用阴道举宫器的患者, 未观察到复发, 而 270 例使用阴道举宫器的患者, 19 例 (7%) 出现复发。有的学者认为举宫器在手术过程中不断挤压肿瘤, 导致肿瘤细胞进入脉管造成肿瘤播散, 应该摒弃举宫器或用非螺旋宫颈托, 禁止旋转。在开腹手术中, 用直角弯钳钳夹肿瘤可以避免肿瘤污染腹腔, 为闭合式手术, 而腹腔镜手术为开放性切开, 反复钳夹肿瘤组织可以造成肿瘤直接污染腹腔。向腹腔充入 CO₂ 形成气腹, 体内 CO₂ 有培养肿瘤细胞增殖的作用, 同时腹腔内 CO₂ 高压, 也会造成腹腔或 TROCA 口肿瘤细胞的种植转移^[24]。我们可以改变腹腔镜手术的操作流程, 在完成腹腔镜下宫旁组织切除术后, 在阴道切断阴道, 将切除组织经阴道取出, 或者在切开阴道前, 先荷包缝合闭合阴道后再离断阴道, 防止肿瘤细胞脱落^[20-21]。在拔出 TROCA 前放空腹腔 CO₂ 或者行无气腹悬吊式腹腔镜手术。要严格冲洗腹腔, 防止肿瘤播散: (1) 43℃ 蒸馏水冲洗: 蒸馏水属于低渗液体, 可以损伤肿瘤细胞膜的通透性; (2) 洗必泰冲洗液: 可以吸附细胞质, 胞浆外渗, 使得细胞内多种酶失活; (3) 碘伏溶液冲洗: 可以预防腹腔感染并防止细胞种植; (4) 抗癌药物溶液: 在生理盐水或者蒸馏水中加入配置的 5-Fu 或 DDP。针对学习曲线问题, 应建立严格的培训制度, 提高准入门槛, 重视手术基本功的训练, 重视无瘤原则的培训, 临床医生的培训应从开腹向腔镜过渡, 选择合适的患者, 分期应 ≤ I B1 期^[25-29]。

综上, 我们更应该重视微创手术的无瘤原则, 包括 (1) 不挤压原则; (2) 隔离原则; (3) 钝性解剖原则; (4) 减少术中扩散原则; (5) 减少癌细胞污染原则; (6) 整块切除原则^[19-23]。

3.2 宫颈癌开腹手术的优势

开腹手术存在的优势有很多: (1) 适应证较广, 包括巨块型; (2) 不需要特殊的器械, 手术时间较短; (3) 复发少, 生存率高; (4) 并发症和中远期生活质量和腹腔镜手术无统计学差异; (5) 泌尿道并发症 (如输尿管瘘、膀胱瘘) 少于腹腔镜手术; (6) 术者有触觉、真实视觉; (7) 止血方便确实、较少热损伤; (8) 切除范围易控制、不需要过度游离; (9) 治疗费用较低; (10) 学习曲线短^[30]。

3.3 宫颈癌腹腔镜手术标本 LVSI 高于开腹手术

病理科医师从手术标本中也注意到了在同等条件下, 腹腔镜手术标本 LVSI 高于开腹手术^[25, 31]。病理科医师曾经在腹腔镜手术病理标本中发现, 宫颈表面鳞状上皮下有淤血的情况, 但不能解释, 整个宫颈间质中血管扩张现象, 并且间质中扩张的血管很多是空虚的, 上述 3 点现象形成一个前提, 癌灶的被动性扩散和局部血管扩张以及开放是有关的。

4 结 语

我们既不能无视研究结果, 也不能完全否定腹腔镜手术治疗宫颈癌的价值, 而是应该从不同角度看待和分析问题, 应当积极开展针对性的研究, 进一步探索微创手术的利和弊, 以及微创手术带来风险的可能原因。需要界定和严格掌握宫颈癌微创手术的适应证: 选择低危病例, 包括宫颈病灶 < 2 厘米、高分化、鳞癌、无深肌层浸润、术前宫颈活检病理无脉管受累等。对这样的“低危”病例亚组, 研究尚未有足够的效能去证明微创手术组和开腹手术组的肿瘤治疗结局是否存在差异。强调腹腔镜手术过程中的无瘤操作, 加强妇科肿瘤医生的培训和建立准入制度, 特别是对施行妇科恶性肿瘤的腹腔镜手术。

综上所述, 目前尚缺乏足够的证据禁止施行宫颈癌的腹腔镜手术, 更不能全面否定腹腔镜在外科手术中的价值; 但是, 也必须正视存在的问题和事实, 积极寻找改进和解决问题的方法。

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