

中低位直肠癌新辅助治疗后全系膜切除术的难点与对策

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【摘要】 局部进展期直肠癌的新辅助放化疗(nCRT)可降低肿瘤局部复发率,使患者生存获益。但nCRT后组织水肿等因素导致组织间隙不清晰,淋巴结清扫和神经保护的难度增加。肿瘤临床完全缓解或接近临床完全缓解后肿瘤下切缘定位困难,以及nCRT后吻合口漏的风险增加等问题,为中低位直肠癌全系膜切除术带来困难和新挑战。笔者结合文献及自身临床经验,总结nCRT后全系膜切除术的难点及对策,以期为同道提供借鉴。

【关键词】 直肠肿瘤; 局部进展期; 新辅助放化疗; 全系膜切除术; 难点; 对策

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Difficulties and strategies of total mesorectal excision for middle and low rectal cancer after neoadjuvant therapy

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【Abstract】 Patients with local advanced rectal cancer (LARC) can benefit from neoadjuvant chemoradiotherapy (nCRT) of reducing local recurrence rate and improving survival rate. However, tissue edema after nCRT may lead to unclear tissue spaces, making it challenging for lymph node dissection and nervous system protection. The difficulty in locating inferior margin of tumor after clinical complete remission or closing to clinical complete remission, as well as the increasing risk of anastomotic leakage after nCRT, pose difficulties and new challenges of total mesorectal excision for middle and low rectal cancer. Based on literatures and clinical experiences, the authors summarize the difficulties and strategies of total mesorectal excision after nCRT, in order to provide reference for colleagues.

【Key words】 Rectal neoplasms; Local advanced; Neoadjuvant chemoradiotherapy; Total mesorectal excision; Difficulties; Strategies

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直肠癌是全世界范围内常见的恶性肿瘤之一。我国确诊的直肠癌中,局部进展期结直肠癌(locally

advanced rectal cancer, LARC)比例较高,其预后相对较差^[1-3]。目前,新辅助放化疗(neoadjuvant chemo-

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radiotherapy, nCRT)+全直肠系膜切除术+术后辅助化疗是中低位 LARC 的标准治疗模式。近年来,国内外众多研究致力于优化 LARC 的 nCRT 模式,以全程新辅助治疗为代表的新模式,可提高局部治疗疗效,增加保肛机会,改善患者术后生命质量,给患者带来生存获益^[4-6]。但 nCRT 影响直肠癌全直肠系膜切除术操作,包括放疗所致的组织水肿或纤维化,导致组织层次间隙不清晰;nCRT 后肿瘤临床完全缓解,致使全直肠系膜切除术术中肿瘤下切缘难以精准判定等问题。笔者结合文献资料和团队临床经验,总结中低位 LARC 行 nCRT 后全直肠系膜切除术操作中的困难和应对措施,旨在为临床实践提供参考。

一、手术方式的选择

选择合理的手术方式可以提高直肠癌 nCRT 后全直肠系膜切除术手术质量,降低手术难度和并发症发生率。随着 4K、3D 及荧光腹腔镜等手术平台的应用,可提升手术视野的显示水平,为复杂及需特殊显影的手术提供保障。3D 腹腔镜系统可提供更好的纵深感及术中操作感,使组织解剖层次和间隙更加清晰。与 2D 腹腔镜比较,3D 腹腔镜手术治疗 nCRT 后直肠癌临床效果满意,后者可提高手术质量^[7]。4K 腹腔镜提供高清晰度手术视野,可呈现局部精细解剖结构,提升手术操作感^[8-9]。在精准导航淋巴结清扫、血管显影和肿瘤定位方面,荧光腹腔镜具有巨大优势^[10-12]。

经肛全直肠系膜切除术(transanal total mesorectal excision, taTME)为直肠癌保肛手术提供新思路。对于肥胖症及盆腔狭窄的低位直肠癌患者,镜下手术视野仍可获得满意暴露,对直肠远切缘的定位也更加精确^[13]。Lu 等^[14]的回顾性研究结果显示:直肠癌患者 nCRT 后施行 taTME 治疗安全可靠,有较好的短期疗效。Shin 等^[15]的研究结果显示:对于接受 nCRT 的直肠癌患者,taTME 和机器人手术系统全直肠系膜切除术的短期预后相似,两种手术方式均可以实现高质量的全直肠系膜切除术。Chen 等^[16]分析 109 例直肠癌患者行 nCRT 后施行机器人手术系统辅助全直肠系膜切除术的肿瘤学结果,中位随访时间为 42 个月,3 年无病生存率和总生存率分别为 73.4% 和 87.2%,疗效较满意。机器人手术系统可突破腹腔镜技术的局限性,三维视觉可放大 10~15 倍,增加视野角度,使手术精确度增加;机器人手术系统可减少手部颤动,“内腕”能以不同角度在靶器官周围操作,特别适合在狭窄空间内操作^[17]。

笔者经验:中低位直肠癌行 nCRT 后患者手术难度增加,建议结合医院实际情况和术者习惯选择合适的术式,以降低手术操作难度,提高手术质量。

二、应对组织间隙不清晰的对策

经过放疗的组织会发生明显水肿或纤维化,使手术视野不清晰,给手术操作带来难度^[18-19]。手术困难主要体现在:(1)应用电刀或超声刀解剖切割组织时,水肿组织可伴随大量液体渗出,形成烟雾附于镜头,导致镜头模糊,影响手术视野观察。(2)盆腔空间常较狭窄,尤其对于男性患者手术视野受到极大限制。(3)如果切除的肿瘤巨大、浸润明显或伴有肠梗阻,将极大增加术中组织显露和手术操作难度。笔者总结以下几项对策:(1)可根据肿瘤情况及术者习惯,选择合适手术入路和合适手术方式。(2)选择合适的能量平台,对于标本侧的出血可以使用双极电凝止血,其效果明显优于超声刀和单极电能量设备^[20]。(3)根据不同解剖部位灵活运用钝性及锐性分离技巧,保持合理对抗牵拉张力,正确扩展层面,可有效减少周围组织损伤。(4)充分发挥吸引器的功能,将渗出液及烟雾及时吸除,保持良好的手术视野,可降低手术难度。

三、淋巴结清扫范围

直肠癌行 nCRT 后施行全直肠系膜切除术,其手术难度将增加^[18,21-22]。直肠癌行 nCRT 后组织水肿、纤维化等变化,导致组织间隙不清晰;肿瘤缓解所致淋巴结缓解,部分淋巴结可能更加隐匿,术中难以及时发现^[23-27]。1 项纳入 21 354 例直肠癌患者的研究结果显示:直肠癌 nCRT 后行手术治疗患者与初始行手术治疗患者比较,前者手术获取的总淋巴结数目明显减少(15.7 枚比 20.0 枚, $P<0.001$),且 N0 分期(淋巴结阴性)患者的占比更高(65.9% 比 49.1%, $P<0.001$)^[28]。笔者经验:可采用荧光显像技术或纳米碳进行淋巴结示踪,可更精确地指导淋巴结清扫范围,并尽可能从手术标本中获取更多淋巴结,从而精准指导肿瘤分期及后续治疗方案的选择。关于直肠癌手术中侧方淋巴结清扫,日本学者认为,全直肠系膜切除+侧方淋巴结清扫术是进展期低位直肠癌的标准手术方式,侧方淋巴结清扫术可降低肿瘤局部复发率^[29]。而西方学者认为:侧方淋巴结清扫术难度大、术后并发症多,可能影响术后排尿和性功能。因此,不推荐行直肠癌侧方淋巴结清扫,主张采用 nCRT 治疗侧方淋巴结转移^[30]。但对于中低位直肠癌,仍有较高比例的患者在 nCRT 后存在侧方淋巴结转移风险^[31-32]。因此,应该选择

性进行侧方淋巴结清扫,对于nCRT后影像学检查仍提示存在侧方淋巴结肿大的患者,应该行侧方淋巴结清扫^[33-35]。

四、植物神经的保护

神经保护对于充分保留患者术后性功能和排尿功能具有重要意义^[36-39]。由于直肠癌行nCRT后导致组织层次间隙不清晰,容易发生盆腔自主神经损伤。术中需按正确的解剖层次进行解剖分离,注重神经的全程保护。(1)骶岬水平的神经保护:该水平腹膜后组织疏松,分离提起乙状结肠系膜过程中常将上腹下神经丛或腹下神经一并提起,容易进入错误间隙发生神经损伤。笔者认为:术中助手需向上适度牵拉,主刀医师逐层切开,准确进入Toldt's间隙,保持Toldt's间隙下方筋膜完整。(2)肠系膜下动脉根部的神经保护:左右腰内脏神经沿腹主动脉两侧走行,处理肠系膜下动脉根部时,左腰内脏神经被其遮挡并被弓形牵拉,故容易损伤。术中可分别从肠系膜下动脉尾侧和头侧拓展Toldt's间隙,再将弓形吊起的左腰内脏神经向背侧推离。可在距肠系膜下动脉根部1 cm处或发出左结肠动脉后离断血管。(3)血管神经束的保护:可从腹膜返折上1~2 cm切开腹膜进入邓氏筋膜前间隙,并在适当的位置(距双侧精囊腺底部0.5 cm)呈“U”字型横断邓氏筋膜前叶,进入邓氏筋膜后间隙,保护血管神经束。(4)下腹下神经丛即盆神经丛的保护:充分拓展直肠后方间隙,沿直肠脏层筋膜向侧方分离,再从直肠前间隙向两侧游离,此时两侧侧韧带会形成菲薄的“膜桥”结构,再自上而下贴紧直肠系膜筋膜切断侧韧带。该过程中应注意适度牵拉暴露,避免过度牵拉导致神经变形误伤或因nCRT后组织脆性增加导致损伤。

五、肿瘤下切缘的定位

直肠癌手术切缘阴性是保障R₀切除的基础。nCRT后直肠病灶缩小,甚至出现接近临床完全缓解或临床完全缓解,肿瘤下切缘的定位比较困难。笔者经验:(1)术前采用肠镜下钛夹定位或联合术中直肠指诊定位,条件允许也可采用术中肠镜检查定位。(2)也可采用吲哚菁绿或纳米碳定位,但需要由丰富注射经验的内镜或外科医师完成,如注射失败反而会增加手术难度。(3)采用taTME或经自然腔道取标本手术I式和II式,可以直视下测量直肠远切缘。

六、吻合口漏的预防

目前,对于新辅助放疗是否会增加术后吻合口

漏的发生率尚未达成共识^[40-43]。但新辅助放疗可能增加直肠癌术后吻合口漏的严重程度,并导致愈合时间延迟^[35]。从放射生物学角度而言,吻合口漏的原因与血管内皮对放射线敏感,同时炎症反应和氧化损伤机制参与,致使放疗引起血管内皮细胞损伤。内皮细胞受损伤后分泌大量黏附因子、炎症分子和趋化因子等,使内皮细胞具有促炎症和促血栓作用,PLT聚集在受损的血管内皮处形成血栓。内皮细胞功能障碍引起通透性增加,进一步促进炎症反应发生。从外科角度而言,吻合口漏的原因与盆腔空间间隙狭小,放疗后造成组织间隙不清晰,容易给直肠远端裸化及闭合造成困难,导致吻合不确切有关。肠管血供是影响吻合口愈合的基本和重要因素之一。目前与高位结扎比较,直肠癌手术中肠系膜下动脉低位结扎降低术后吻合口漏发生率尚存在争议^[44-47]。而对存在Riolan动脉弓缺如、Griffiths吻合薄弱或缺如等血管变异患者,直肠癌术后发生吻合口漏的风险增加已达成共识^[48]。

笔者建议:对于高龄、一般情况较差、存在动脉硬化或存在肠系膜血管变异等患者,应尽可能保留左结肠动脉,以保障吻合口良好血供。也可采用术中吲哚菁绿荧光成像评估结直肠手术中吻合口血运^[11-12]。预防性造口及关闭盆底腹膜可能不会直接降低吻合口漏发生率,但可以降低因吻合口漏导致的严重腹腔感染率^[49]。加固缝合吻合口及消除双吻合中形成的“狗耳朵区”,可降低吻合口漏发生率^[50]。我国1项多中心RCT结果显示:对于未行nCRT的中低位直肠癌患者,放置肛管不会降低吻合口漏发生率^[51]。而放置肛管能否降低nCRT后吻合口漏发生,需高质量研究验证。笔者团队近年来采用PAPV模式,即预防性造口(preventive stoma)+留置肛管(indwelling anal canal)+关闭盆底腹膜(close the pelvic floor peritoneum)+保留左结肠血管(left colonic blood vessels),以降低吻合口漏发生率^[52]。国内也有学者报道采用PAPV模式显著降低腹腔镜低位直肠癌吻合口漏发生率^[53]。

七、结语

随着LARC治疗策略的不断优化,临床完全缓解率得到有效提升,对于未获得临床完全缓解患者,仍然需要进行全直肠系膜切除术。而部分临床完全缓解患者因采取观察等待策略,而取得较长的器官保留时间,但也存在肿瘤复发风险,肿瘤复发后需要施行补救性全直肠系膜切除术。因此,对于LARC,nCRT后行全直肠系膜切除术仍不可或缺。

笔者建议:外科医师需要继续探索 nCRT 各种优化模式下施行全直肠系膜切除术的策略。

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