世界华人消化杂志®
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世界华人消化杂志 2006年8月8日; 14(22): 2247-2250
ISSN 1009-3079 CN 14-1260/R

CLINICAL PRACTICE

新辅助化放疗在局部进展期低位直肠癌保留肛门括约肌的作用

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收稿日期: 2006-05-29 接受日期: 2006-06-19

Role of sphincter preserving surgery with neoadjuant chemoradiotherapy for locally advanced low rectal cancer

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Received: 2006-05-29 Accepted: 2006-06-19

Abstract

AIM: To evaluate the role of the sphincter preserving surgery with neoadjuvant chemoradiotherapy in locally advanced low rectal cancer.

METHODS: Forty-two patients with T3 and T4 low rectal cancer were treated by pre-operative radiotherapy to pelvis, 2 Gy daily up to 40-46 Gy in 4 weeks concomitantly with oral administration of capecitabine (CAP) at 1250 mg/m^2 bid for 10 weeks (group A). Twenty-one patients were treated by the same chemoradiotherapy after operation (group B).

RESULTS: Neoadjuvant chemoradiotherapy (NCR) was successfully completed in group A. Among the 42 patients, tumor lesions disappeared in 5 cases, so they didn't receive operation. Curative resection was carried out in the remaining 37 patients, of which 33 received the sphincter-saving resection (SSR) and 4 received abdomino-perineal resection (APR). The rate of sphincter preservation was 89.2% in group A. Of the 21 patients in group B, 11 received SSR and 10 received APR. The rate of sphincter preservation was 52.4% in group B.

CONCLUSION: NCR shows high efficacy in tumor down-staging and shrinkage of tumor mass, and improves the resection rate and sphincter preservation.

Key Words: Rectal cancer; Neoadjuant chemoradiotherapy; Sphincter preserving resection

Luo Q, Zhang SE, Wei LY. Role of sphincter preserving surgery with neoadjuant chemoradiotherapy for locally advanced low rectal cancer. Shijie Huaren Xiaohua Zazhi 2006;14(22):2247-2250

摘要

目的:

.

方法: 2002-10/2006-02 T3, T4
63 A 42 ,
40-46 Gy/20-23 , 5 /wk, 2 Gy/ ,
1250 mg/(m^2·d), 2 ,
, 6 wk
; B 21 , ,
.

结果: A , 5
, . 37 ,
33 , 4
, A 89.2%. B
21 , 11
, 10 ,
52.4%.

结论: ,
.

关键词 ; ;

罗琪, 张颂恩, 魏黎煜. 新辅助化放疗在局部进展期低

■背景资料
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■研发前沿
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位直肠癌保留肛门括约肌的作用. 世界华人消化杂志 2006;14(22):2247-2250
http://www.wjgnet.com/1009-3079/14/2247.asp

0 引言

低位直肠癌是大肠癌中最好发、最难治、疗效最差的一类. 随着手术技术和手术器械的发展, 直肠癌保留肛门括约肌的比例不断提高[1-3]. 但低位局部进展期直肠癌保留肛门括约肌的手术仍是目前外科治疗的难点. 为了使更多的低位局部进展期直肠癌患者生活质量的提高, 保住肛门[4], 我科2002-10/2006-02对局部进展期低位直肠癌患者42例先施行新辅助化放疗后再行经腹直肠癌切除, 经肛门结肠肛管吻合的保留肛门括约肌的手术, 叙述如下.

1 材料和方法

1.1 局部进展期低位直肠癌63例, 男39例, 女24例; 年龄16-72(平均52±0.5)岁. 患者均经直肠指诊、结肠镜、腹部B超和盆腔CT扫描, 部分患者经直肠腔内B超等检查, 临床判断为T_3, T_4期的经病理学检查确诊. 按2∶1比例分组. 一组行术前新辅助化放疗后手术, 术后常规化疗6周期(A组). 二组确诊后即行手术, 术后常规化疗6周期(B组). 肿瘤下缘距肛缘5-6.5(平均5.9)cm. 肿瘤T_3期51例, T_4期12例(按照国际TNM分期法[5]), 溃疡型36例, 隆起型22例, 绒毛状腺瘤癌变5例(按中国抗癌协会制定的大肠癌大体分型), 肿瘤细胞中高分化(Ⅰ-Ⅱ级)53例, 低分化(Ⅲ级)10例.

1.2 每日给予卡培他滨1250 mg/m^2. 化疗(瑞士罗氏公司提供)分2次口服, 自放疗开始不间断口服至手术. 术前放射治疗剂量为40-46 Gy, 分次剂量为1.8-2 Gy/d, 每周5 d, 休息2 d, 共4-5 wk完成. 放疗结束后休息6 wk再决定是否手术. 放疗后5 wk复查直肠指诊、结肠镜、腹部B超、盆腔CT、大肠癌肿瘤标志物(CEA, CA19-9等)、部分患者直肠腔内B超. 根据结果按WHO标准对治疗结果进行评定, 确定手术方案. 本组病例不论是术前辅助化放疗组, 还是先手术再化疗组, 手术操作无论是保留肛门括约肌或腹会阴切除术均按TME操作规范进行, 其中A组21例行双吻合器(美国强生公司提供)吻合保留肛门括约肌, 12例按Parks法行肛门结肠吻合保留肛门括约肌.

用SPSS 11.5统计分析软件包进行分析处理, 统计分析方法为χ^2检验和t检验.

2 结果

新辅助化放疗组(A组)术前经10 wk的辅助化放疗, 当术前再次检查时(包括直肠指诊、纤维结肠镜、盆腔CT、部分患者直肠腔内B超等检查)发现5例肿瘤完全消失, 未行手术继续给予随访观察. 余37例施行根治性肿瘤切除, 其中33例行保留肛门括约肌手术, 4例行腹会阴切除术, 新辅助化放疗组保肛率89.2%. 未行新辅助化放疗组(B组), 21例行根治性肿瘤切除, 其中11例行保留肛门括约肌手术, 10例行腹会阴切除术, B组保肛率52.4%. A组病理结果与新辅助化放疗前比较, 达CR(肿瘤完全消失)6例, 加上经新辅助化放疗肿瘤完全消失未手术的5例, 故达CR的为11例(26.2%), PR(肿瘤部分缓解)22例(占52.4%), SD(病情稳定)9例, ORR(总有效率)为78.6%. 病理分期为$T_1N_0$15例, $T_2N_0$15例, $T_3N_0$4例, $T_{2-3}N_1$3例. B组病理分期$T_3N_0$13例, $T_{2-3}N_1$8例. 两组其他资料基本相同有可比性.

A组在化疗期间2例出现轻度的手足综合征, 1例腹泻经处理均完成新辅助治疗, 全组无围手术期死亡, 均获随访, 随访时间2-40(中位18)mo. A组在随访期间发现局部复发2例, 肝转移1例, 肺转移1例, 复发转移率为10.8%. 随访期间暂无死亡, 故无复发生存或无瘤生存率为89.2%. B组随访期间发现局部复发3例, 肝转移1例, 腹腔内广泛转移2例, 复发转移率为28.6%, 无复发生存或无瘤生存率为71.4%

有所提高[11-12]. 本组病例经新辅助治疗, 收到了较好的疗效. 在化疗期间2例出现轻度的手足综合征, 1例腹泻经处理均完成新辅助治疗, 全组无围手术期死亡. 89.2%(33例)保留肛门括约肌, 随访2-40 mo局部复发2例. 出现肝转移1例, 肺转移1例. 病理判断达CR占26.2%(11例), PR占52.4%(22例), ORR78.6%; 病理分期从治疗前的T_3-T_4期变为T_1-T_3期. 而未行新辅助治疗组保留肛门手术仅52.4%, 随访局部复发转移率为28.6%(6/21), 死亡2例. 两组无复发转移生存率比较t = 0.813, P<0.01有非常显著差异, 证实新辅助治疗对进展期直肠癌能达到降期和降低局部复发的目的.

新辅助放疗是直肠癌主要辅助治疗手段之一[13], **他能很好地预防直肠癌局部复发, 提**高手术切除率, 增加保肛率, 提高生存质量和生存率[14-15]. 新辅助放疗是达到肿瘤降期很有效的方法. 放射线对癌细胞的作用包括直接作用和间接作用[16]. 直接作用的靶点是DNA分子链, 导致细胞核内DNA的单链断裂, 双链断裂. 间接作用是射线和组织细胞内的原子或分子相互作用产生的自由基, 造成DNA的间接损伤. 照射所致细胞死亡的敏感部位在核内, 术前放疗使肿瘤退缩. 降低分期的另一主要原因是诱导直肠癌细胞增加凋亡, 明显抑制癌细胞的增殖[17]. 癌细胞增殖速度越快、增殖比率越大放射治疗效果越好. 新辅助放疗相对术后放疗最主要区别在于术前放疗可使肿瘤缩小、降期, 更有利于手术操作, 可使非常低位的肿瘤施行保留肛门括约肌手术[18]. 因而术前放疗的生存率明显高于术后放疗; 同时术前放疗可使保留肛门括约肌手术的成功率明显提高, 改善生活质量[19]. 术前放疗要注意两点: (1)剂量要适度, 剂量太大影响手术, 剂量太小达不到肿瘤降期的目的. 我们使用的剂量是40-46 Gy, 分次剂量为1.8-2 Gy/d, 每周5 d, 休息2 d, 共4-5 wk完成. 此剂量属中等剂量, 患者耐受好, 无明显不良反应, 全组患者均完成放疗; (2)结束放疗后需休息4-6 wk再手术[20], 目的是待放射的组织反应消退, 同时充分发挥放射治疗对肿瘤的杀伤作用, 达到肿瘤缩小、**降期的目的. 过早地进**行手术可能增加手术困难和手术并发症. 我们的经验是放疗后6 wk手术比4 wk好, 降低了手术操作的难度, 提高了保肛手术的成功率.

近年来的研究, 从理论上和实践上证实了下段直肠癌保留肛门括约肌手术的合理性和可行性[21]. 手术技术和器械的改进和发展, 使直肠癌保留肛门括约肌手术从40%左右增至目前的70%左右. 辅助治疗最大限度提供了直肠癌根治的机会. 直肠癌根治切除必须遵循公认的TME操作规范[22-25], 在保证切净局部病灶和区域淋巴结的前提下, 切除肿瘤远侧2-3 cm的正常肠管. 有些病人切除肿瘤后盆底肌上残留的直肠不足2 cm或虽长于2 cm但无法使用双吻合器行保留肛门括约肌手术. 我们应用1972年Parks[26]提出的经腹直肠癌切除经肛门结肠肛管吻合的术式, 使12例超低位直肠癌患者成功地保留肛门括约肌. 实践证明此术式可以弥补双吻合器技术在低位直肠癌保留肛门括约肌手术中的不足, 术后经肛门功能锻炼, 术后”新直肠”逐渐代偿性扩张, 肛门功能在6-12 mo后可基本恢复正常. 本研究表明, 局部进展期低位直肠癌采用新辅助化疗与放疗联合应用可使疗效发挥至最大. 虽然术后肠道功能会受到一定的影响, 并发症可能会有一定的增加, 但肿瘤根治性切除率明显提高, 术后局部复发率明显降低, 对局部进展期低位直肠癌治疗是一种较好的治疗方法.

■应用要点

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■名词解释

■ 同行评价

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