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射波刀立体定向放疗技术治疗结直肠癌肝转移癌的疗效观察*

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摘要 目的:探讨射波刀立体定向放疗技术治疗结直肠癌肝转移癌的疗效观察。**方法:**选择2014年1月至2016年2月我院收治的64例结直肠癌肝转移癌患者为研究对象,按照随机数字表法随机分为对照组(32例)和治疗组(32例),对照组患者给予FOLFOX6全身化疗方案,治疗组患者给予FOLFOX6全身化疗和肝脏病灶立体定向放疗(射波刀)治疗。观察患者的治疗3个月后的近期临床疗效和不良反应,6个月后患者生存率和局部控制率,并评价患者的生活质量。**结果:**治疗3个月后,治疗组患者的总有效率为78.13%,高于对照组的53.13%,差异有统计学意义(P<0.05);治疗6个月后,治疗组的生存率(96.88%)和局部控制率(87.50%)均高于对照组(81.25%和65.63%),差异有统计学意义(P<0.05);治疗6个月后,治疗组患者的情绪功能、认知功能、角色功能、躯体功能、社会功能评分均高于对照组,差异有统计学意义(P<0.05)。两组患者的不良反应发生率比较差异无统计学意义(P>0.05)。**结论:**射波刀立体定向放疗技术治疗结直肠癌肝转移癌具有较好的近期临床疗效,可提高患者的生存率和局部控制率,改善患者生活质量,且不良反应发生率低,值得临床推广应用。

关键词:结直肠癌;肝转移癌;射波刀;立体定向放疗;生活质量

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Clinical Efficacy of Cyberknife Stereotactic Body Radiotherapy Technology on Treatment of Colorectal Cancer Liver Metastatic Carcinoma*

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ABSTRACT Objective: To study the clinical efficacy of cyberknife stereotactic body radiotherapy technology on treatment of colorectal cancer liver metastatic carcinoma. **Methods:** 64 patients with colorectal cancer liver metastatic carcinoma were divided into control group (32 cases) and treatment group (32 cases), according to random number table method, in our hospital from January 2014 to February 2016. The control group was given FOLFOX6 systemic chemotherapy regimens, and the treatment group was given cyberknife stereotactic body radiotherapy combined with FOLFOX6 systemic chemotherapy. After 3 months the recent clinical curative effect and adverse reaction were observed. After 6 months the survival rate, local control and patient's quality of life were evaluated. **Results:** After 3 months treatment, the total effective rate 78.13% in treatment group was higher than that of the control group 53.11%, the difference was statistically significant (P<0.05). After 6 months of treatment, the survival rate (96.88%) and local control rate (87.50%) of the treatment group were significantly higher than those in the control group (65.63% and 81.25%), and the difference was statistically significant (P<0.05); After 6 months of treatment, the emotional function, cognitive function, role function, physical function and social function score of the treatment group were higher than those of the control group, the difference was statistically significant (P<0.05). There was no significant difference in the incidence of adverse reactions between the two groups (P>0.05). **Conclusion:** Radio wave knife stereotactic radiotherapy technology for the treatment of colorectal liver metastases cancer has better clinical effect in the near future, can improve the survival rate and local control rate,improve the quality of life of patients, and the incidence of adverse reactions was low, it is worthy of clinical application.

Key words: Colorectal cancer; Liver metastasis; Radio wave knife; Stereotactic radiotherapy; Quality of life

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前言

随着经济发展和生活水平的提高,结直肠癌发病率逐年上升,成为严重威胁生命健康的常见恶性肿瘤[1,2]。结直肠癌极易发生肝转移,多数为多发转移瘤,无法行手术切除治疗,且伴有腹水、肝区疼痛及肝脏功能异常等,严重影响患者的生活质量,是结直肠癌患者死亡的主要原因[3-5]。结直肠癌肝转移癌的治疗主要为全身化疗(FOLFOX6 、FOLFIRI 等联合化疗方案)、局部

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放疗、射频治疗等非手术治疗方法[6]。射波刀立体定向放疗技术具有局部剂量高,周围正常组织受量低特点,可对全身肿瘤立体定向放射治疗,已广泛应用于肺癌、脑肿瘤等治疗,具有较好的临床疗效[7-9]。本研究旨在探讨射波刀立体定向放疗技术对结直肠癌肝转移癌的临床疗效及其不良反应。

1 资料与方法

1.1 临床资料

选择 2014 年 1 月至 2016 年 2 月我院收治的 64 例结直肠癌肝转移癌患者为研究对象,所有患者均经 CT 或 MRI 检查或病理确诊为直肠癌肝内转移癌，无手术指征或拒绝手术治疗者，肝内转移肿瘤数量小于 4 个，最大径小于 5cm 患者,KPS 评分大于 60 分,患者预期坚持放疗结束,预期生存时间大于 3 个月。排除直肠癌肝外转移患者,合并其他恶性肿瘤患者,妊娠或哺乳期妇女,心肝肾等重大疾病及精神疾病患者,不接受射波刀立体定向放疗者。按照随机数字表法随机分为对照组(32 例)和治疗组(32 例),两组患者的一般临床资料比较(P>0.05),具可比性。见表 1。

表 1 两组一般资料的比较

Table 1 Comparison of general data in two groups

Items	Control group (n=32)	Treatment group (n=32)	x^2/t	P
Sex(M/F)	17/15	19/13	0.673	0.564
Age (year)	63.82± 5.53	64.11± 5.65	-0.284	0.817
Tumor types (colon/rectum)	21/11	20/12	0.336	0.847
Pathologic types(glandular cancer /squamous carcinoma)	25/7	24/8	0.314	0.862
Tumor number(n)	2.13± 0.59	2.21± 0.62	-0.215	0.884
KPS score(score)	68.76± 6.41	69.32± 7.31	-0.523	0.648
BMI(kg/m^2)	24.11± 3.52	23.47± 3.41	0.667	0.529

1.2 治疗方法

对照组患者给予 FOLFOX6 全身化疗方案，奥沙利铂(50 mg/ 支,浙江海正药业股份有限公司,生产批号:20131019)85 mg/m^2 静脉输注 2 h,亚叶酸钙(0.1 g/ 支,广东岭南制药有限公司，生产批号:20131105)200 mg/m^2 静脉输注 2 h,5-FU(0.25 g/10 mL,天津金耀药业有限公司,批号:20130915) 400 mg/m^2 推注,然后 5-FU 2400 mg/m^2 静脉输注 46 h,每 3 周 1 疗程。如患者 12 月内已行 FOLFOX6 全身化疗方案，给予 FOLFIRI 化疗方案,将奥沙利铂改为伊立替康(100 mg/5 mL,江苏恒瑞医药股份有限公司,生产批号:20130927)350 mg/m^2。治疗组患者给予 FOLFOX6 全身化疗和肝脏病灶立体定向放疗（射波刀）治疗,采用射波刀立体定向放射平台治疗,采用 Synchrony 追踪系统对肿瘤进行追踪放疗。放疗前 1 周 CT 引导下穿刺植入金标 1~4 枚,治疗时真空气垫固定患者治疗体位,行 1 mm 强化 CT 定位扫描。肿瘤靶区为影像资料显示肝转移灶,计划靶区为肿瘤靶区外扩 5 mm，根据病灶大小采用单靶点或多靶点照射，50％剂量线覆盖计划靶区，95%以上肿瘤靶区 80％~90％剂量包裹。肝转移治疗处方剂量为 50%剂量线，计划靶区外器官最大剂量小于处方剂量，为 5~6 Gy/ 次,1 次 /2d,共 5~6 次,总剂量为 30 ~40 Gy。

1.3 观察指标

治疗 3 个月后,参照 RECIST 肿瘤疗效判断标准进行疗效判断[4],完全缓解(CR):所有靶病灶消失;部分缓解(PR):靶病灶的最大直径总和减少 30%;稳定(SD):病灶缩小未达 PR 或增加未达 PD;进展(PD):病灶的最大直径总和增加 20%或出现新病灶为。总有效率 =(CR+PR)/ 总例数× 100%。治疗 6 个月后,根据 RECIST 标准对肝转移局部控制情况评价,局部控制(local control , LC)为自放疗开始至肿瘤局部进展,新出现转移,放疗病灶未进展,计算局部控制情况。生存期(overall survival, OS)为自放疗开始至随访截止患者死亡情况。不良反应根据 NCICT-CAE 3.0 进行评估[10]。采用生存质量量表(QLQ-C30)[8]评价生活质量(情绪功能、认知功能、角色功能、躯体功能、社会功能),每项 100 分,分值高说明生存质量较高。

1.4 数据分析

数据以 SPSS19.0 统计分析,n(%)表示计数资料,χ^2 检验;以（$\bar{X}$± S）表示计量资料,t 检验比较组内和组间差异,P<0.05 为检验标准。

2 结果

2.1 近期临床疗效比较

治疗组患者的总有效率为 78.13%,高于对照组的 53.13%,差异有统计学意义(χ^2=4.433,P=0.035),见表 2。

表 2 两组临床疗效比较[n(%)]

Table 2 Comparison of clinical efficacy in two groups[n(%)]

Groups	CR	PR	SD	PD	Total efficiency
Control group (n=32)	5(15.63)	12(37.50)	9(28.13)	6(18.75)	17(53.13)
Treatment group (n=32)	9(28.13)	16 (50.00)	5 (15.63)	2(6.25)	25(78.13) *

NOTE: Compared with control group, *P<0.05.

2.2 生存率和控制率比较

治疗组的生存率、局部控制率(87.50%)均高于对照组,差异有统计学意义(χ^2=4.010、4.267,P=0.045、0.039)。见表 3。

表 3 两组患者生存率和局部控制率比较[n(%)]

Table 3 Comparison of survival rate and local control rate in two groups[n(%)]

Groups	n	Survival rate	Local control rate
Control group	32	26(81.25)	21(65.63)
Treatment group	32	31(96.88)	28(87.50)*

NOTE: Compared with control group, *P<0.05.

2.3 生活质量比较

治疗组患者的情绪功能、认知功能、角色功能、躯体功能、社会功能评分均高于对照组(P<0.05)。见表 4。

表 4 两组患者生活质量的比较(分)

Table 4 Comparison of quality of life in two groups(score)

Groups	Emotive function	Cognitive function	Role function	Physical function	Social function
Control group(n=32)	51.32± 11.24	49.63± 11.84	51.53± 12.73	42.73± 10.58	54.47± 12.35
Treatment group(n=32)	60.42± 12.45	57.36± 12.71	58.62± 12.75	54.47± 11.28	61.53± 12.14
t	3.069	3.555	2.226	4.294	2.306
P	0.002	0.000	0.015	0.000	0.012

2.4 不良反应比较

对照组患者发生腹泻 5 例、恶心呕吐 4 例、肝功能异常 2 例,治疗组患者发生腹泻 4 例、恶心呕吐 4 例、肝功能异常 3 例、放射性胃溃疡 2 例。治疗组的不良反应发生率 40.63%(13/32)与对照组比较 34.38%(11/32),差异无统计学意义(x^2=0.267,P=0.606)。

3 讨论

结直肠肿瘤是消化道常见恶性肿瘤,极易发生肝转移,出现腹水和肝功能异常,严重影响患者生存时间及生活质量。结直肠癌肝转移癌患者已失去手术治疗最佳时机,另外由于手术治疗创伤较大,不利于患者的预后恢复,对患者的生活质量提高不明显,不作为首选治疗方法[10,11]。化疗及放疗是治疗结直肠癌肝脏转移的常用方法,新辅助化疗 FOLFOX6 以 5-FU 为基础,配合亚叶酸钙,配合奥沙利铂,治疗结直肠癌肝转移疗效好,患者能耐受[12]。放疗经历了全肝、局部疗、全肝移动条放疗、超分割放疗后,近年来立体定向放疗技术逐渐应用于肝癌治疗,立体定向放疗技术通过对灶区实施大剂量照射,肿瘤靶区具有高放射剂量,可以降低靶区周围正常组织照射剂量,可保护正常组织,适用于全身各部位肿瘤的治疗[13,14]。本研究选择 64 例结直肠癌肝转移癌患者为研究对象,旨在探讨射波刀立体定向放疗技术治疗结直肠癌肝转移癌的临床疗效,为其治疗提供参考。

射波刀立体定向放疗技术治疗肝转移癌患者通过植入金标,真正达到图像引导的立体定向放疗,根据肿瘤部位可调整放疗剂量,提高临床疗效。本研究发现,治疗组患者的总有效率高于对照组。说明射波刀立体定向放疗技术治疗结直肠癌肝转移癌具有较好的临床疗效。亚叶酸钙能增强 5-FU 生物活性,延长 5-FU 对胸苷酸合成酶的抑制,调节 5-FU 代谢,奥沙利铂对许多耐顺铂或卡铂细胞具有活性,与 5-FU 有明显的协同作用[15]。射波刀立体定向放疗采用 50%剂量线,使靶区内剂量分布梯度增大,肿瘤区可获得更高的剂量[16]。治疗 6 个月后,治疗组生存率 96.88%和局部控制率 87.50%均高于对照组 81.25%和 65.63%,差异有统计学意义。说明射波刀立体定向放疗技术治疗结直肠癌肝转移癌可控制局部肿瘤,提高患者生存率。射波刀立体定向放疗因肿瘤靶区剂量高、周边计划靶区剂量较小的特点,具有较高局部控制率,在放疗转移灶时对其周围组织可能存在的亚临床病灶也有治疗作用,降低了内复发率[17]。治疗 6 个月后,治疗组患者的情绪功能、认知功能、角色功能、躯体功能、社会功能等生活质量评分高于对照组,差异有统计学意义。说明射波刀立体定向放疗技术治疗结直肠癌肝转移癌可提高患者的生活质量。这是由于射波刀立体定向放疗具有较好的临床疗效,可控制局部肿瘤,提高患者生存率有关[18]。而 FOLFOX6 全身化疗奥沙利铂与 5-FU 协同增效,破坏 DNA 的结构和功能抑制的协同效果,抗癌谱扩大,提高了结肠癌患者的生存状况[19]。两组患者的不良反应主要为腹泻、恶心呕吐、肝功能异常、放射性胃溃疡等,治疗组的不良反应发生率 40.63%(13/32)与对照组比较 34.38%(11/32),差异无统计学意义。说明射波刀立体定向放疗技术治疗结直肠癌肝转移癌不良反应较低,患者可以耐受,安全性较好[20]。

综上,射波刀立体定向放疗技术在治疗结直肠癌肝转移癌方面有较好的近期临床疗效,可提高患者的生存率和局部控制率,改善患者生活质量,且不良反应发生率低,值得临床推广应用。

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(上接第 779 页)

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