

影像引导后期加速超分割调强适形放疗联合奈达铂治疗食管癌的临床观察

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摘要: [目的] 观察影像引导后期加速超分割放疗联合奈达铂化疗治疗食管癌的有效性及安全性。[方法] 2016年1月至2017年3月60例食管癌初治患者按照随机数字表法分为后期加速超分割放疗联合奈达铂化疗(观察组)和后期加速超分割放疗联合多西他赛+顺铂化疗(对照组), 各30例, 放疗采用影像引导调强适形精确放疗技术, 6MV-X线, 4~5个共面或非共面适形照射野, 前期GTV和GTVnd总剂量44Gy, 2.2Gy/次, 共20次, CTV总剂量36Gy, 1.8Gy/次, 共20次, 5次/周; 后期GTV和GTVnd总剂量18Gy, 1.5Gy/次, 共12次, CTV总剂量13.2Gy, 1.1Gy/次, 共12次。化疗: 观察组单药奈达铂40mg/m²静脉滴注, 放疗期间1次/周。对照组: 多西他赛60mg/m²静脉滴注d₁, 顺铂25mg/m²静脉滴注d₁₋₃, 放疗第1、28天开始化疗。比较两组近期有效率、不良反应发生率、局控率和生存率。[结果] 两组近期疗效评价差异无统计学意义(P>0.05); 观察组与对照组中位局部控制时间分别为(24.0±4.1)个月(95%CI: 15.9~32.1)和(26.0±2.2)个月(95%CI: 21.7~30.2), 1-、2-、3-年局部控制率分别为80.0%、53.3%、33.3%和76.7%、63.3%、36.7%($\chi^2=0.575$, P=0.448), 中位生存期分别为(27.0±3.4)个月(95%CI: 20.4~33.6)和(32.0±3.0)个月(95%CI: 26.2~37.8), 1-、2-、3-年生存率分别为83.3%、66.7%、40.0%和86.7%、70.0%、46.7%($\chi^2=0.425$, P=0.515)。观察组心脏、肾脏和放射性食管炎不良反应发生率均低于对照组(P=0.036、0.038、0.032), 胃肠道反应及血液学不良反应无差异。[结论] 影像引导后期加速超分割调强适形放疗同步奈达铂周化疗治疗食管癌有效性与后期加速超分割放疗同步多西他赛联合顺铂方案相似, 安全性更优于放疗同步两药联合方案。

关键词: 食管肿瘤; 后期加速超分割; 影像引导; 调强放疗; 同步放化疗

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Image-guided Late Course Accelerated Hyperfraction Intensity-Modulated Radiotherapy Combined with Nedaplatin Chemotherapy for Esophageal Cancer

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Abstract: [Purpose] To observe the efficacy and safety of image-guided late course accelerated hyperfraction intensity-modulated radiotherapy(IG-LCAHFIMRT) combined with nedaplatin chemotherapy in the treatment of esophageal cancer. [Methods] From January 2016 to March 2017, 60 patients with esophageal cancer were randomly divided into two groups: IG-LCAHFIMRT combined with nedaplatin chemotherapy (study group) and IG-LCAHFIMRT combined with docetaxel + cisplatin chemotherapy (control group) with 30 cases in each group. Radiotherapy was performed with image-guided intensity-modulated conformal precision radiotherapy, 6MV-X lines, 4 or 5 coplanar or non-coplanar conformal radiation fields. The first course with conventional fraction for GTV and GTVnd 44Gy, 2.2Gy per fraction, 20 fractions, CTV 36Gy, 1.8Gy per fraction, 20 fractions, 5 fractions per week, later course with hyperfraction for GTV and GTVnd 18Gy, 1.5Gy per fraction, 12 fractions, CTV 13.2Gy, 1.1Gy per fraction, 12 fractions. The study group received nedaplatin 40mg/m² i.v., once/week during radiotherapy, while the control group received docetaxel 60mg/m²/day i.v. on d₁, cisplatin 25mg/m² was injected intravenously on d₁₋₃, and chemotherapy began on the d₁ and d₂₈

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of radiotherapy. The short-term efficacy rate, incidence of adverse reactions, local control rate and survival rate were compared between the two groups. [Results] There was no significant difference in short-term efficacy between the two groups ($P>0.05$). The median local control time of the study group and the control group was 24.0 ± 4.1 months (95%CI:15.9~32.1) and 26.0 ± 2.2 months (95%CI:21.7~30.2), and the 1-, 2- and 3-year local control rates were 80.0%, 53.3%, 33.3% and 76.7%, 63.3%, 36.7% respectively ($\chi^2=0.575$, $P=0.448$). The median survival time was 27.0 ± 3.4 months (95%CI:20.4~33.6) and 32.0 ± 3.0 months (95%CI:26.2~37.8), and the 1-, 2- and 3-year survival rates were 83.3%, 66.7%, 40.0% and 86.7%, 70.0%, 46.7%, respectively ($\chi^2=0.425$, $P=0.515$). The incidence of adverse reactions in heart, kidney and radiation esophagitis in the study group was lower than that in the control group ($P=0.036, 0.038, 0.032$), but there was no significant difference in gastrointestinal reactions and hematological adverse reactions. [Conclusion] The efficacy of IG-LCAHFIMRT combined with nedaplatin chemotherapy in the treatment of esophageal cancer is similar to that of IG-LCAHFIMRT combined with docetaxel and cisplatin, but the incidence of adverse reactions is less.

Key words: esophageal cancer; late course accelerated hyperfractionation; image guidance, intensity modulation radiotherapy; concurrent chemoradiotherapy

食管癌是我国乃至全球的高发和高致死性恶性肿瘤之一^[1-2]。放射治疗在食管癌的治疗中具有重要的作用^[3],同步放化疗更是作为局部晚期不可手术食管癌的标准治疗手段^[4]。然而,常规分割放射治疗疗效多年来难以突破,施学辉等^[5]开展的后程加速超分割放射治疗使食管癌的5年生存率提高到30%左右,Zhao等^[6]报道后程加速超分割同步氟尿嘧啶联合顺铂方案治疗食管癌,5年生存率40%,随着精确放疗技术的进展及新型化疗药物的临床可及,新技术引导下的后程加速超分割放疗及同期化疗方案的选择仍需进一步研究。我们采用影像引导后程加速超分割调强适形放疗(image-guided late course accelerated hyperfraction intensity-modulated radiotherapy, IG-LCAHFIMRT)联合奈达铂(nedaplatin, NDP)周化疗治疗食管癌,疗效可靠,安全性高,现报道如下。

1 资料与方法

1.1 临床资料

本研究选取就诊于甘肃省肿瘤医院行放射治疗的食管癌初治患者60例,纳入标准:①经组织或细胞病理证实为食管癌的初治患者,病理类型不限;②年龄18~75岁;③能流质饮食;④卡氏评分 ≥ 60 分,预期生存期大于6个月;⑤食管病灶长度 ≤ 10 cm,胸下段食管癌无锁骨上淋巴结转移及远隔转移;⑥无食管穿孔前征象;⑦血常规、心脏、肝脏和肾

脏等脏器功能均正常。排除标准:①合并第二原发肿瘤者;②八周内接受过包括放射治疗、化学治疗或手术治疗等其他治疗;③食管完全梗阻不能进食流质饮食;④食管有深溃疡或穿孔或呕血;⑤使用其他实验药物或参加其他临床试验的患者;⑥有不可控制的癫痫发作或因精神疾病丧失自知能力者;⑦研究者认为不宜参加本试验者。

采用随机数字表法随机分为影像引导后程加速超分割调强适形放疗联合奈达铂周化疗30例(IG-LCAHFIMRT+NDP)(试验组)和影像引导后程加速超分割调强放疗联合多西他赛+顺铂(Docetaxel+Cisplatin)化疗30例(IG-LCAHFIMRT+TP)(对照组)。本研究开始前获得甘肃省肿瘤医院伦理委员会许可备案,患者入组前已充分知情,并签署知情同意书。两组患者基线情况可比(Table 1)。

1.2 治疗方法

1.2.1 放疗

采用影像引导调强适形放疗技术;6MV-X线;体位固定使用热塑体膜或头颈肩膜固定装置,CT扫描范围从环状软骨到膈肌下5cm,建议使用静脉造影剂(对确有使用造影剂禁忌者行CT平扫),扫描层厚5mm。勾画靶区时参照MRI或PET-CT确定肿瘤靶区(gross target volume, GTV)或转移淋巴结靶区(gross target volume node, GTVnd)。按照ICRU62号报告(1999)^[7]确定靶区, GTV包括所有通过CT、PET、食管片和食管镜等检查发现的食管肿瘤。转移淋巴结的定义(≥ 1 项):PET阳性;CT影像上短

径 $\geq 1\text{cm}$ (气管食管沟淋巴结短径 $\geq 0.5\text{cm}$);穿刺证实为转移者。临床靶区(clinical target volume,CTV)包括 GTV 头脚方向外放 3cm,前后左右外放 0.5cm,

外放后 GTVnd 未纳入 CTV 时,需在 GTVnd 外放 0.5cm 构成相应 CTV,勾画时注意避开椎体和心、肺脏器。计划靶区(plan target volume,PTV):为 CTV 四周或上下均外放 0.5cm。

Table 1 Clinical characteristics of 60 cases with esophageal cancer

Features	IG-LCAHFIMRT +NDP group (30 cases)	IG-LCAHFIMRT +TP group (30 cases)	χ^2	P
Gender				
Male	25(83.3%)	26(86.7%)	0.131	0.718
Female	24(41.4%)	20(35.7%)		
Age(years)				
≤ 50	5(16.7%)	3(10.0%)	1.425	0.490
50~70	17(56.7%)	15(50.0%)		
≥ 70	8(26.7%)	12(40.0%)		
Pathological types				
Squamous cell carcinoma	28(93.3%)	27(90.0%)	1.018	0.601
Adenocarcinoma	2(6.7%)	2(6.7%)		
Small cell carcinoma	0	1(3.3%)		
Tumor location				
Cervical and upper	15(50.0%)	12(40.0%)	1.111	0.574
Middle	10(33.3%)	14(46.7%)		
Lower	5(16.7%)	4(13.3%)		
Primary tumor length(cm)				
≤ 5	7(23.3%)	10(33.3%)	0.739	0.390
5~10	23(76.7%)	20(66.7%)		
Tumor stage				
T ₁	6(20.0%)	7(23.3%)	1.553	0.670
T ₂	10(33.3%)	6(20.0%)		
T ₃	13(43.3%)	15(50.0%)		
T ₄	1(3.3%)	2(6.7%)		
Nodal stage				
N _x	8(26.7%)	10(33.3%)	0.606	0.739
N ₀	4(13.3%)	5(16.7%)		
N ₁	18(60.0%)	15(50.0%)		
Clinical stage				
I	3(10.0%)	5(16.7%)	1.989	0.738
II a	5(16.7%)	3(10.0%)		
II b	8(26.7%)	11(36.7%)		
III	12(40.0%)	10(33.3%)		
IV a	2(6.7%)	1(3.3%)		
Histological grade				
Well	12(40.0%)	15(50.0%)	0.630	0.730
Moderately	14(46.7%)	12(40.0%)		
Poorly	4(13.3%)	3(10.0%)		
KPS				
60~80	14(46.7%)	10(33.3%)	1.111	0.292
≥ 80	16(53.3%)	20(66.7%)		
Weight loss before therapy				
<10%	23(76.7%)	19(63.3%)	1.270	0.260
$\geq 10\%$	7(23.3%)	11(36.7%)		

Notes:NDP;nedaplatin;TP;docetaxel+cisplatin

剂量分割采用同步加量后程加速超分割,前程常规分割:GTV 和 GTVnd 总剂量 44Gy,2.2Gy/次,共 20 次,CTV 总剂量 36Gy,1.8Gy/次,共 20 次,5 次/周;后程加速超分割:GTV 和 GTVnd 总剂量 18Gy,1.5Gy/次,共 12 次,CTV 总剂量 13.2Gy,1.1Gy/次,共 12 次,2 次/d,2 次间隔>6h。后程依据放疗中期相关影像学检查,若肿瘤退缩明显,则行二次定位;将前后程计划采用 MIM 系统融合,结合剂量体积直方图和靶区云图评价计划,要求处方剂量覆盖 95%的 GTV 和 GTVnd 体积,同时 GTV 和 GTVnd 体积内不得存在 $\geq 110\%$ 的剂量热点,双肺平均剂量<14Gy, $V_{20}\leq 28\%\sim 30\%$, $V_{30}<20\%$;心脏 $V_{40}<30\%$;脊髓最大点剂量<45Gy。

1.2.2 化疗

试验组同步化疗采用单药奈达铂(NDP)(先声药业,11-180507,规格 10mg)40mg/m² 静脉滴注,放疗期间 1 次/W;对照组化疗采用多西他赛+顺铂(TP)方案:多西他赛(恒瑞医药,批号:H20020543)60mg/m²,静脉滴注,d₁,顺铂(齐鲁制药,批号:H20023461)25mg/m²,静脉滴注,d₁₋₃,放疗第 1、28 天开始化疗,共 2 个周期。化疗的当日仍进行放射治疗;并给予化疗前预防过敏、止吐、保肝、利尿等支持治疗。

所有患者在根治性放化疗后接受 2~4 个周期辅助化疗,化疗方案采用多西他赛联合奈达铂方案:多西他赛(恒瑞医药,批号:H20020543)75mg/m²,静脉滴注,d₁,奈达铂(NDP)(先声药业,11-180507,规格 10 mg)100mg/m² 静脉滴注,d₁。

1.2.3 不良反应处理

治疗期间出现放射性食管炎者给

予药物减轻黏膜水肿/糜烂对症治疗, 咽喉疼痛影响进食者给予鼻饲饮食。 ≥ 2 级骨髓抑制者给予相应药物对症治疗。当出现 > 3 级心、肺和 > 4 级血液系统毒性时, 暂停治疗。

1.3 有效性评价

1.3.1 近期疗效评价标准

分别于放疗前、放疗总剂量至 40Gy、放疗结束及结束后 1~3 个月复查食管造影及颈胸腹部 CT。近期疗效依据国内万钧教授提出的食管癌近期疗效评定标准评价为完全缓解 (complete response, CR)、部分缓解 (partial response, PR)、疾病稳定 (stable disease, SD) 或疾病进展 (progressive disease, PD), 以 CR+PR 计算近期总有效率^[8]。

1.3.2 远期疗效

放化疗结束后 6 个月内原病变部位出现病灶者为局部未控, 6 个月后局部出现病灶者为肿瘤复发; 通过治疗后随访获得 1-、2-、3-年局控率及 1-、2-、3-年生存率。

1.4 安全性评价

根据 CTCAE V3.0 版对药物不良事件进行评价。放射治疗相关不良反应按照美国放射治疗肿瘤协作组 (radiation therapy oncology group, RTOG) 放射损伤分级标准进行评价^[9]。

1.5 统计学处理

统计软件采用 SPSS 21.0。所有统计检验均为双侧, P 值取小于或等于 0.05 为差异有统计学意义; 定量指标的描述将计算均值、标准差、中值、最小值和最大值。所述分类索引和各种类型描述的病例数的百分比; 分别计算两组数据, 采用 Kaplan-Meier 方法, Log-rank 检验对两组生存资料数据进行统计。

2 结果

2.1 治疗及随访情况

2016 年 1 月至 2017 年 3 月, 按照纳入排除标准, 在甘肃省肿瘤医院完成患者入组。试验组最高放疗剂量为 62Gy, 最低剂量为 52Gy。对照组最高放疗剂量为 62Gy, 最低剂量为 56Gy。观察组同步化疗完成率 100%, 辅助化疗分别为 4 周期 20 例 (66.7%), 3 周期 6 例

(20.0%), 2 周期 3 例 (10.0%), 1 例 (3.3%) 因同步放化疗不良反应明显未行辅助化疗; 对照组 1 例患者完成 1 周期同步化疗, 辅助化疗分别为 4 周期 16 例 (53.3%), 3 周期 4 例 (13.3%), 2 周期 5 例 (16.7%), 1 周期 2 例 (6.7%), 3 例 (10.0%) 因同步放化疗不良反应明显未行辅助化疗。2019 年 12 月 31 日为末次随访时间, 试验组失访 1 例, 随访率 96.7%, 对照组随访率 100%。失访按死亡计算。

2.2 近期疗效

放化疗结束后 3 个月, 根据患者临床症状、体格检查、食管造影及 CT 进行疗效评价。CR、PR、SD 试验组分别为 60.0%、20.0%、16.7%, 对照组分别为 76.7%、10.0%、13.3%; 试验组 PD 1 例 (3.3%), 近期总有效率 (CR+PR) 分别为 80.0% 和 86.7% ($P>0.05$) (Table 2)。

2.3 两组 1-、2-、3-年局部控制率和生存率比较

试验组和对照组中位局部控制时间分别为 (24.0 $\pm$ 4.1) 个月 (95%CI: 15.9~32.1) 和 (26.0 $\pm$ 2.2) 个月 (95%CI: 21.7~30.2); 1-、2-、3-年局控率试验组分别为 80.0%、53.3%、33.3%; 对照组分别为 76.7%、63.3%、36.7%, 差异无统计学意义 ($\chi^2=0.575$, $P=0.448$); 两组中位生存时间分别为 (27.0 $\pm$ 3.4) 个月 (95%CI: 20.4~33.6) 和 (32.0 $\pm$ 3.0) 个月 (95%CI: 26.2~37.8); 1-、2-、3-年生存率试验组分别为 83.3%、66.7%、40.0%; 对照组分别为 86.7%、70.0%、46.7%, 差异无统计学意义 ($\chi^2=0.425$, $P=0.515$) (Figure 1、2)。

2.4 两组不良反应发生率比较

试验组消化道反应如恶心、呕吐发生率及严重程度均低于对照组, 但差异无统计学意义 (P 分别为 0.064 和 0.184); 观察组未观察到心脏和肾毒性, 对照组心脏和肾毒性发生率分别为 20% 和 13.3% ($P=0.036$, 0.038); 血液系统不良反应两组差异无统计学

Table 2 Comparison of short-term curative effects between LCAHFIMRT+NDP group and LCAHFIMRT+TP group

Features	IG-LCAHFIMRT +NDP group (30 cases)	IG-LCAHFIMRT +TP group (30 cases)	χ^2	P
CR	18(60.0%)	23(76.7%)	1.926	0.165
PR	6(20.0%)	3(10.0%)	1.176	0.278
SD	5(16.7%)	4(13.3%)	0.131	0.718
PD	1(3.3%)	0	1.017	0.313
CR+PR	24(80.0%)	26(86.7%)	0.480	0.488

Notes: NDP: nedaplatin; TP: docetaxel+cisplatin

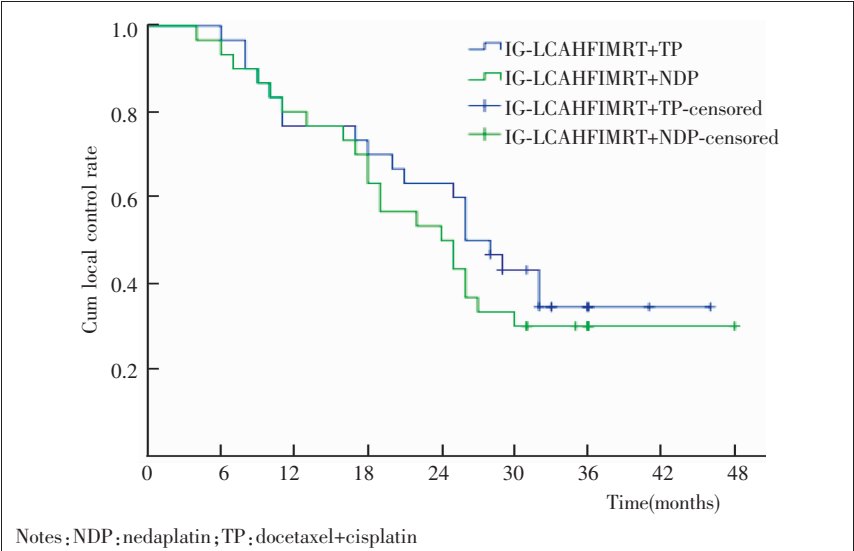


Figure 1 Comparison of 1-,2-,3-year local control rates between IG-LCAHFIMRT+NDP group and IG-LCAHFIMRT+TP group

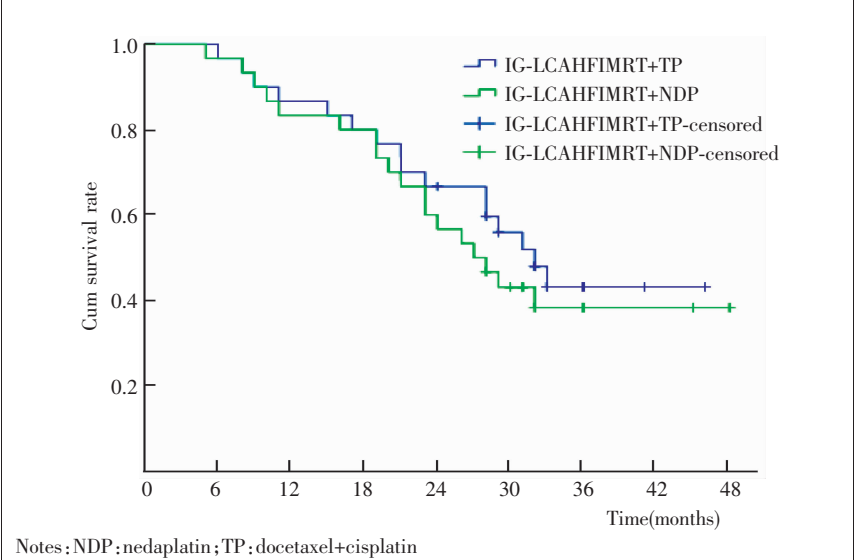


Figure 2 Comparison of 1-,2-,3-year survival rates between LCAHFIMRT+NDP group and LCAHFIMRT+TP group

意义；放疗相关性不良反应方面：两组 2 级以上放射性肺炎发生率分别为 23.3%和 30.0% ($P=0.607$)；放射性食管炎两组发生率分别为 40.0%和 76.7% ($P=0.032$) (Table 3)。

3 讨论

放射治疗是食管癌局部治疗的主要手段之一,然而多年的临床实践表明常规分割放射治疗食管癌疗效不理想,5 年生存率仅 15%左右,失败的主要原因为局部/区域未控和复发^[10]。实验研究显示,多种动物移植肿瘤和若干人体肿瘤,尤其是头颈部和上呼吸道、上消化道鳞癌在常规

Table 3 Comparison of treatment side effects between LCAHFIMRT+NDP group and LCAHFIMRT+TP group

Types of side effect	IG-LCAHFIMRT+NDP group (30 cases)					IG-LCAHFIMRT+TP group (30 cases)					χ^2	P
	0	1	2	3	4	0	1	2	3	4		
Nausea	20 (66.7%)	8 (26.7%)	2 (6.7%)	0	0	10 (33.3%)	14 (46.7%)	5 (16.7%)	1 (3.3%)	0	7.255	0.064
Vomiting	26 (86.7%)	3 (10.0%)	1 (3.3%)	0	0	20 (66.7%)	7 (23.3%)	3 (10.0%)	0	0	3.383	0.184
Heart	30 (100.0%)	0	0	0	0	24 (80.0%)	5 (16.7%)	1 (3.3%)	0	0	6.667	0.036
Kidney	30 (100.0%)	0	0	0	0	26 (86.7%)	4 (13.3%)	0	0	0	4.286	0.038
Reduce of WBC	10 (33.3%)	12 (40.0%)	5 (16.7%)	3 (10.0%)	0	8 (26.7%)	9 (30.0%)	8 (26.7%)	3 (10.0%)	2 (6.7%)	3.343	0.502
Reduce of PLT	17 (56.7%)	7 (23.3%)	3 (10.0%)	2 (6.7%)	1 (3.3%)	15 (50.0%)	7 (23.3%)	8 (26.7%)	0	0	5.398	0.249
Radiation pneumonitis	14 (46.7%)	9 (30.0%)	5 (16.7%)	2 (6.7%)	0	9 (30.0%)	12 (40.0%)	5 (16.7%)	3 (10.0%)	1 (3.3%)	2.716	0.607
Radiation esophagitis	18 (60.0%)	8 (26.7%)	3 (10.0%)	1 (3.3%)	0	7 (23.3%)	18 (60.0%)	4 (11.7%)	1 (3.3%)	0	8.829	0.032

Notes: NDP: nedaplatin; TP: docetaxel+cisplatin; WBC: white blood cell; PLT: platelet

分割放疗过程中,存活肿瘤干细胞在治疗后期发生加速再增殖现象,可能是导致常规分割放疗失败的主要原因^[11]。以后程加速超分割为主的非常规分割放疗理论上可以抑制肿瘤干细胞受照射后加速再增殖现象,但因二维放疗时代的大野照射会引发较多的并发症,并且我国医疗资源的紧缺,使这一技术在临床的推广受到限制。三维适形放射治疗(3-dimensional conformal radiotherapy, 3-DCT)通过 TPS 计划系统可以使照射野形状与肿瘤形状保持一致,从而减少正常组织受照射面积;Wang 等^[12]报道三维适形后程加速超分割放疗治疗食管癌的 1-、2-、3-年生存率分别为 79.2%、56.3%和 43.8%,优于常规分割放疗;王敏等^[13]采用后程加速超分割三维适形放疗同步紫杉醇联合顺铂治疗 60 例食管癌患者,有效率 88.3%,1 年、2 年局部控制率分别为 74.3%、58.7%,1 年、2 年生存率分别为 66.7%、55.0%,优于三维适形常规分割放疗联合化疗组。调强适形放射治疗(intensity-modulated radiotherapy, IMRT)通过逆向计划系统调节照射野内各点输出剂量率,确保靶区内部及表面剂量处处相等的适形照射方式,其优点是能在更大程度上减少正常组织和器官的照射剂量^[14],因此,IMRT 可减少放疗后期的副作用。另外由于可实现安全推量,从而进一步提高了肿瘤的局控率^[15-16]。王修身等^[17]报道经采用 3-CDT、IMRT 精确放疗同步化疗,颈段食管癌的 5 年总生存率达到 33.2%。本研究通过对 60 例食管癌患者采用影像引导后程加速超分割调强适形放射治疗联合化疗,无论是两药联合方案,还是单药周化疗方案,均显示出了较好的局部控制率和长期生存率,略优于既往文献报导的研究结果^[12-13],这可能得益于精确放疗技术减少了摆位误差、器官移动等造成靶区移位的因素,提高了肿瘤靶区的辐射剂量^[18],同时通过后期加速超分割技术抑制了肿瘤干细胞在放疗后期的加速再增殖。

基于 RTOG 随机 III 期临床试验,同期放化疗成为局部晚期食管癌的非手术治疗标准方案^[19-20]。顺铂为基础的两药联合化疗为当前各大指南推荐的食管癌同步化疗方案,后程加速超分割放疗同步顺铂为基础的两药联合化疗可增加急性放射性食管炎,增加食管穿孔风险,同时由于顺铂的胃肠道不良反应及肾毒性,降低了临床治疗的依从性^[6,12-13]。奈达铂是第二代铂类抗肿瘤制剂,主要通过抑制 DNA 的复制达到抗肿瘤作用,与顺铂的抗癌作用机制相同,

研究显示其胃肠道反应及黏膜反应较顺铂低,对鳞癌有较好的治疗效果^[21],现已广泛应用于肺癌、食道癌、头颈癌的治疗,特别是在顺铂、卡铂不耐受或耐药的情况下^[22]。奈达铂作为周化疗放疗增敏方案,在多种实体瘤特别是老年患者的治疗中显示出了较好的疗效和耐受性^[23-25]。本研究显示后期加速超分割放疗联合奈达铂周化疗致胃肠道反应(恶心、呕吐)发生率为 33.3%和 13.3%,低于放疗同步多西他赛联合顺铂化疗方案(67.7%和 33.3%),但差异未达统计学意义,这可能与本研究中多西他赛联合顺铂方案组将顺铂总量分三天给予,一定程度上降低了胃肠道毒性反应有关;奈达铂单药周化疗组未出现心脏及肾脏不良反应,而这在多西他赛联合顺铂联合化疗方案组分别为 20.0%和 13.3%;两组均存在不同程度的血液学不良反应,主要为 I~III 度白细胞、血小板降低,差异无统计学意义,经给予 G-CSF 和 IL-11 治疗后恢复正常,不影响后续治疗;放射性肺炎两组 2 级以上需临床干预者发生率相似;放射性食管炎总体发生率奈达铂周化疗组为 40.0%,低于多西他赛联合顺铂化疗组 76.7%($P=0.032$),差异有统计学意义,这提示放疗联合奈达铂周化疗具有较轻的食管黏膜损伤,对于提高同步放化疗依从性具有实际临床意义。

综上,影像引导后期加速超分割调强适形放疗同步奈达铂周化疗治疗食管癌有效性与后期加速超分割放疗同步多西他赛联合顺铂方案相似,安全性更优于放疗同步两药联合方案。这为临床实际工作中合理选择化疗方案,降低过度治疗所带来的不良反应具有一定的指导意义。鉴于本研究样本量偏少,且不排除在研究实施过程中可能存在的混杂因素造成的偏倚,因此尚需进一步开展大样本量、多中心前瞻性随机对照研究探讨后期加速超分割放疗的同步化疗方案这一临床问题。

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