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三维适形放疗治疗食管鳞癌的近期疗效、生存率及预后的影响因素分析*

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摘要 目的: 观察三维适形放疗治疗食管鳞癌的近期疗效、生存率并分析其预后的影响因素。**方法:** 纳入我院从2010年11月~2016年10月收治的食管鳞癌患者150例进行研究,按治疗方式的不同分成研究组($n=84$,三维适形放疗治疗)和常规组($n=66$,常规放疗治疗)。随访3年,比较两组近期疗效、毒副反应发生情况以及3年生存情况。单因素分析研究组患者3年生存情况与性别、年龄、病变长度、病变部位、大体肿瘤体积(GTV)的关系,多因素 Logistic 回归分析三维适形放疗食管鳞癌患者预后的影响因素。**结果:** 研究组治疗总有效率显著优于常规组($P<0.05$)。研究组放射性食管损伤、血液毒性反应发生率均显著低于常规组(均 $P<0.05$)。研究组1、2、3年存活率均显著高于常规组(均 $P<0.05$)。单因素 Logistic 分析结果显示:不同年龄、病变长度、病变部位以及 GTV 的食管鳞癌患者三年生存率比较差异有统计学意义(均 $P<0.05$)。多因素 Logistic 回归分析发现年龄 ≥ 70 岁、病变长度 ≥ 50 mm、病变部位为胸下段、 $GTV \geq 40 \text{ cm}^3$ 均是三维适形放疗食管鳞癌患者3年内死亡的危险因素。**结论:** 三维适形放疗治疗食管鳞癌患者的近期疗效优于常规放疗,可降低毒副反应发生率,提高生存率。年龄 ≥ 70 岁、病变长度 ≥ 50 mm、病变部位为胸下段、 $GTV \geq 40 \text{ cm}^3$ 均是三维适形放疗食管鳞癌患者3年内死亡的危险因素,值得临床重点关注。

关键词: 食管鳞癌; 三维适形放疗; 疗效; 生存率; 预后; 毒副反应; 大体肿瘤体积

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Analysis of the Factors Influencing the Short-term Efficacy, Survival Rate and Prognosis of Three-dimensional Conformal Radiotherapy for Esophageal Squamous Cell Carcinoma*

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ABSTRACT Objective: To observe the short-term efficacy, survival rate and prognostic factors of three-dimensional conformal radiotherapy for esophageal squamous cell carcinoma. **Methods:** 150 patients with esophageal squamous cell carcinoma who were admitted to our hospital from October 2010 to October 2016 were included in the study. The patients were divided into study group ($n=84$, three-dimensional conformal radiotherapy) and conventional group ($n=66$, conventional radiotherapy) according to different treatment methods. The patients were followed up for 3 years, the short-term efficacy, toxic side effects and 3-year survival rate of the two groups were compared. Single factor Logistic analysis was performed to analyze the relationship between the 3-year survival of the study group and gender, age, lesion length, lesion site and gross tumor volume (GTV). Multivariate Logistic regression analysis was performed to analyze the prognostic factors of patients with esophageal squamous cell carcinoma. **Results:** The total effective rate in the study group was significantly higher than that in the conventional group (all $P<0.05$). The incidence of radioactive esophageal injury and hemotoxic reaction in the study group were significantly lower than those in the conventional group (all $P<0.05$). The 1-year, 2-years and 3-years survival rates in the study group were significantly higher than those in the conventional group (all $P<0.05$). Univariate Logistic analysis found that there were statistically significant differences in 3-year survival rates among patients with esophageal squamous cell carcinoma at different ages, lesion length, lesion site and GTV (all $P<0.05$). Multivariate Logistic regression analysis showed that age ≥ 70 years, lesion length ≥ 50 mm, lesion site was lower thoracic segment and $GTV \geq 40 \text{ cm}^3$ were risk factors for 3-year mortality of esophageal squamous cell carcinoma after three-dimensional conformal radiotherapy. **Conclusion:** The short-term effect of three-dimensional conformal radiotherapy on patients with esophageal squamous cell carcinoma is better than conventional radiotherapy, which can reduce the incidence of adverse reactions and improve the survival rate. Age ≥ 70 years, lesion length ≥ 50 mm, lesion site is lower thoracic segment, and $GTV \geq 40 \text{ cm}^3$ are all risk factors for death of patients with esophageal squamous cell carcinoma after

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three-dimensional conformal radiotherapy within 3 years, which are worthy of clinical attention.

Key words: Esophageal squamous cell carcinoma; Three-dimensional conformal radiotherapy; Efficacy; Survival rate; Prognosis; Toxic side effects; Gross tumor volume

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前言

食管癌属于全球范围内最为常见的一种恶性肿瘤,具有发病率高、预后差、死亡率高的特点,我国临床上绝大部分患者均为鳞状细胞癌,对射线敏感度较高,因此放射治疗应用于食管癌治疗中效果明显,是目前临床上应用较为广泛的食管鳞癌治疗手段之一^[1,2]。既往传统放疗因受到肺受量与心脏受照体积的影响,因而病变食管局部剂量的提高受到限制,从而使得患者生存率相对较低,预后不良^[3,4]。三维适形放疗技术的应用可在一定程度上减少对肿瘤邻近器官、组织的照射剂量,同时增加了肿瘤部位的剂量,可更为有效地提高肿瘤局部控制率^[5,6]。然而,三维适形放疗治疗后仍有部分食管鳞癌患者病灶无法得到有效控制,最终死亡^[7,8]。鉴于此,本文通过研究三维适形放疗治疗食管鳞癌的近期疗效、生存率及预后的影响因素,旨在为三维适形放疗应用于食管鳞癌治疗中提供理论依据,并为改善患者预后提供参考依据,现作以下报道。

1 资料与方法

1.1 一般资料

选取 2010 年 11 月~2016 年 10 月我院收治的食管鳞癌患者 150 例进行研究,将其按照治疗方式的不同分成研究组 84 例和常规组 66 例。研究组男 56 例,女 28 例,年龄 33~88 岁,平均年龄(71.22±10.93)岁;肿瘤部位:胸上中段 70 例,胸下段 14 例;大体肿瘤体积(Gross tumor volume, GTV)情况: < 40 cm³ 40 例, ≥ 40 cm³ 44 例。常规组有男 44 例,女 22 例,年龄 35~88 岁,平均年龄(71.30±10.94)岁;肿瘤部位:胸上中段 57 例,胸下段 9 例, GTV 情况: < 40 cm³ 32 例, ≥ 40 cm³ 34 例。两组上述指标比较,差异无统计学意义($P>0.05$),均衡可比。纳入标准:(1)所有研究对象均经病理组织活检确诊为食管鳞癌^[9];(2)均拟行放疗治疗;(3)年龄 ≥ 18 周岁;(4)未发现远处转移;(5)入院前尚未接受相关抗肿瘤治疗。排除标准:(1)合并其它恶性肿瘤者;(2)意识障碍或伴有精神疾病者;(3)研究过程中因各种原因退出者。纳入对象或其家属均在知情同意书上签字,并获批于我院伦理委员会。

1.2 治疗方法

常规组实施常规放疗,采用 X 线模拟机实施定位,治疗靶

区按照食管钡餐造影以及胸部 CT 检查等结果选取。以 " 一前两后 " 斜野等中心照射技术, 6MV X 线照射, 2.0Gy/ 次, 1 次/d, 5 次/周。靶区剂量控制在 50~66Gy 之间, 分 25~33 次完成。研究组则实施三维适形放疗, 患者均取仰卧位, 采用美国 GE BrightSpeed Elite Select 16 排多功能螺旋 CT 模拟定位机增强扫描, 层厚取 5 mm。将扫描所获取的图像通过光盘或局域网传导输入美国 CMS. XIO 三维适形治疗计划系统(Treatment planning system, TPS)实施三维重建, 按照 ICRU50 号以及 62 号报告定义进行 GTV、临床靶体积 (Clinical target volume, CTV) 以及计划靶体积 (Planned target volume, PTV) 的勾画, 同时勾画邻近危及器官, 其中 GTV 即为 CT 所显示的肿瘤大小与肿大淋巴结, CTV 则是 GTV 左右前后方向延长 0.5~1.0 cm, 上下方向延长 2.5~3.0 cm, PTV 则是 CTV 外放 0.5 cm。设计 4-6 个共面或非共面适形野, 用 95% 等剂量线包括并以此等剂量线作为处方剂量, 处方剂量取 50~70Gy, 分 25~35 次完成, 分割方式与常规组一致。危及器官限量: 两肺 V20 ≤ 25%、V30 ≤ 20%, 脊髓剂量 ≤ 45Gy。借助西门子直线加速器 6MV X 线完成治疗。两组视患者耐受情况治疗 5-8 周。

1.3 观察指标

比较两组近期疗效、毒副反应发生情况以及生存率。对所有患者均进行为期 3 年的随访观察, 以电话或上门的方式完成随访, 随访频率为 1 月/次, 若患者死亡则随访终止。统计随访期间两组患者的生存情况。于所有患者治疗 4 周后参照下述评估标准进行^[10], 包括完全缓解、部分缓解、无缓解, 将完全缓解、部分缓解人数和与总人数的百分比记作总有效率。毒副反应主要包括放射性食管损伤、血液毒性反应。

1.4 统计学方法

数据的分析借助 SPSS20.0 软件完成, 计量资料以($\bar{x} \pm s$)表示, 行 t 检验; 计数资料以[n(%)]表示, 行 χ^2 检验。单因素分析三维适形放疗食管鳞癌患者 3 年生存情况与临床各指标的关系, 多因素 Logistic 回归分析三维适形放疗食管鳞癌患者预后的影响因素。 $P<0.05$ 表示差异显著性。

2 结果

2.1 两组近期疗效对比

研究组近期疗效显著优于常规组($P<0.05$), 见表 1。

表 1 两组近期疗效对比[n(%)]

Table 1 Comparison of short-term efficacy between the two groups [n(%)]

Groups	n	Complete remission	Partial remission	No remission	Total effective rate
Study group	84	39(46.43)	35(41.67)	10(11.90)	74(88.10)
Conventional group	66	28(42.42)	21(31.82)	17(25.76)	49(74.24)
χ^2	-				4.805
P	-				0.028

2.2 两组毒副反应发生情况对比

研究组放射性食管损伤、血液毒性反应(均为 1-2 级)发生率分别为 69.05%(58/84)、70.24%(59/84), 均显著低于常规组的 86.36%(57/66)、89.39%(59/66) ($\chi^2=6.195$ 、 8.081 ; $P=0.013$ 、 0.004)。

2.3 两组 1、2、3 年存活率对比

研究组 1、2、3 年存活率分别为 82.14%(69/84)、65.48%(55/84)、45.24%(38/84), 均显著高于常规组的 68.18%

(45/66)、48.48%(32/66)、28.79%(19/66) ($\chi^2=3.950$ 、 4.380 、 4.245 ; $P=0.047$ 、 0.036 、 0.039)。

2.4 三维适形放疗食管鳞癌患者 3 年生存情况的单因素 Logistic 分析

经单因素 Logistic 分析发现:三维适形放疗食管鳞癌患者 3 年生存情况的影响因素包括年龄、病变长度、病变部位以及 GTV(均 $P<0.05$),见表 2。

表 2 三维适形放疗食管鳞癌患者 3 年生存情况的单因素 Logistic 分析[n(%)]

Table 2 Single factor Logistic analysis of 3-year survival of patients with esophageal squamous cell carcinoma after three-dimensional conformal radiotherapy [n(%)]

Factors		Death group(n=38)	Survival group(n=46)	χ^2	P
Gender	Male	23(60.53)	33(71.74)	1.177	0.278
	Female	15(39.47)	13(25.00)		
Age(years)	< 70	17(44.74)	32(69.57)	5.278	0.022
	≥ 70	21(55.26)	14(30.43)		
Lesion length(mm)	< 50	24(63.16)	17(36.96)	5.718	0.017
	≥ 50	14(36.84)	29(63.04)		
Lesion site	Upper and middle thoracic segment	27(71.05)	43(93.48)	7.535	0.006
	Lower thoracic segment	11(28.95)	3(6.52)		
GTV(cm ³)	< 40	25(65.79)	15(32.61)	9.185	0.002
	≥ 40	13(34.21)	31(67.39)		

2.5 三维适形放疗食管鳞癌患者预后的多因素 Logistic 回归分析

以患者预后情况为因变量(赋值存活 =0,死亡 =1),年龄、病变长度、病变部位以及 GTV 为自变量,自变量赋值情况如下:年龄<70 岁 =0,≥ 70 岁 =1;病变长度<50 mm=0,≥ 50

mm=1;病变部位胸上中段 =0,胸下段 =1;GTV<40 cm³=0,≥ 40 cm³=1。经多因素 Logistic 回归分析发现:年龄≥ 70 岁、病变长度≥ 50 mm、病变部位为胸下段、GTV≥ 40 cm³ 均是三维适形放疗食管鳞癌 3 年死亡的危险因素,见表 3。

表 3 三维适形放疗食管鳞癌预后的多因素 Logistic 回归分析

Table 3 Multivariate logistic regression analysis of the prognosis of esophageal squamous cell carcinoma after three-dimensional conformal radiotherapy

Factors	β	SE	Wald χ^2	P	OR	95%CI
Age≥ 70 years	0.014	0.005	4.203	0.011	1.140	1.007~1.204
Lesion length ≥ 50 mm	0.193	0.091	3.011	0.018	1.203	1.094~1.315
Lesion site was lower thoracic segment	0.142	0.057	3.975	0.032	1.744	1.495~1.935
GTV≥ 40 cm ³	0.008	0.001	7.304	0.000	1.482	1.104~1.682

3 讨论

食管癌属于临床上较为常见的消化系统恶性肿瘤之一,手术是迄今为止临床所公认的唯一可治愈手段,但因患者发病早期临床症状不典型,大部分患者一经确诊便已是中晚期,丧失了手术根治的时机,加之其对射线较为敏感,因此放疗已成为食管癌的重要治疗手段之一^[11,12]。然而,不少研究报道证实,常规放疗的效果并不十分理想,患者死亡率亦难以得到有效控制^[13-15]。且由于食管形状呈反 S 形,加之其与周围组织器官的关系较为密切,从而使得常规食管钡餐透视模拟定位难以显示食

管腔外肿瘤的状况,无法进一步准确判断照射野的大小以及照射中心,影响了对病灶的精确诊断,最终增加了局部复发率^[16]。

本文结果发现:研究组的总有效率显著优于常规组,这和阿合力·纳斯肉拉等人的研究结果相符^[17],说明三维适形放疗治疗食管鳞癌的近期疗效更优,分析原因,我们认为三维适形放疗主要是通过 CT 模拟定位,同时实施三维 TPS 设计个体化治疗方案,可相对完整地对靶区进行照射,促使放疗高剂量分布的立体形态与靶区相适合^[18-20]。与此同时,该放疗方案可实现精准放疗,从而在最大程度上避免对脊髓、肺等重要器官造成不必要的损伤,促使 90%的等剂量线包含全部 PTV,进一步提

高了靶区剂量,减少正常组织的受量,继而发挥提高局部肿瘤控制效果的目的^[21-23]。研究组放射性食管损伤、血液毒性反应发生率均显著低于常规组,这与 Lin 等人的研究结果相吻合^[24],表明了三维适形放疗应用于食管鳞癌的治疗中具有较高的安全性。究其原因,我们认为可能和该放疗方式有效避免对邻近器官以及组织造成不必要损伤有关。此外,研究组 1、2、3 年存活率均显著高于常规组,这提示三维适形放疗应用于食管鳞癌治疗可显著提高患者的生存率,其中主要原因可能是三维适形放疗为肿瘤周围正常组织提供保护的同时,还保障了靶区的处方剂量,从而使得肿瘤靶区剂量分布更为合理,有助于提升局部控制效果^[25],进一步提高了生存率。本文结果还发现年龄 ≥ 70 岁、病变长度 ≥ 50 mm、病变部位为胸下段、GTV ≥ 40 cm³ 均是三维适形放疗食管鳞癌 3 年死亡的危险因素,这在孟凡军等人的研究结果中可以得到佐证^[26],分析原因,可能是随着患者年龄的不断增长,机体抵抗力随之减退,放疗耐受力降低,加之其普遍伴有一种或多种基础疾病,继而不利于病情控制。病变长度的增加,表明患者病情更为严重,增加了临床治疗的难度,因此预后往往较差^[27,28]。此外,胸上中段肿瘤患者因病变部位的解剖学结构限制其于病灶较小、病变时间较短时即实施放疗,而胸下段患者往往为手术筛选后病例,其病变程度较重,从而使得放疗后产生的放射性损伤较大,修复能力下降,因而预后不良的风险,同时 GTV 的增加亦会增加放疗使用的剂量,从而患者放射性损伤加重,影响预后^[29,30]。

综上所述,三维适形放疗应用于食管鳞癌的治疗中的近期效果优于常规放疗,可在一定程度上提高 3 年生存率,减少毒副作用,年龄 ≥ 70 岁、病变长度 ≥ 50 mm、病变部位为胸下段、GTV ≥ 40 cm³ 的食管鳞癌患者经三维适形放疗治疗后的食管癌患者 3 年内死亡的风险较高,应予以重视。

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