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食管癌调强放疗并发放射性肺损伤的危险因素分析*

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摘要 目的:分析食管癌调强放疗并发放射性肺损伤的危险因素。**方法:**以2015年2月-2018年2月于青海医学院附属医院接受调强放疗的食管癌患者100例为研究对象。分别收集患者年龄、性别、吸烟史、同步化疗情况、卡氏评分、肿瘤分期等资料以及放射剂量学因素V5、V10、V20、V30、Dmean情况,并采用单因素和多因素Logistic回归分析分析食管癌调强放疗并发放射性肺损伤的危险因素。**结果:**100例患者中发生放射性肺损伤人数为27例,发生率为27.00%。其中1级20例,2级7例。经单因素分析可得:食管癌调强放疗并发放射性肺损伤与卡氏评分、V5、V10、V20、V30以及Dmean有关($P<0.05$);与性别、年龄、吸烟史、同步化疗、肿瘤分期无关($P>0.05$)。经多因素Logistic回归分析可得:卡氏评分 <80 分、 $V5\geq 60\%$ 、 $V10\geq 40\%$ 、 $V20\geq 25\%$ 、 $V30\geq 20\%$ 、 $Dmean\geq 10\%$ 均是食管癌调强放疗患者并发放射性肺损伤的独立危险因素($P<0.05$)。**结论:**食管癌调强放疗并发放射性肺损伤的发生率较高,且与卡氏评分以及放射剂量学因素V5、V10、V20、V30、Dmean密切相关。临床工作中可通过控制肺组织的照射剂量,减少放射性肺损伤发生风险。

关键词:食管癌;调强放疗;放射性肺损伤;危险因素

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Risk Factors Analysis of Radioactive Lung Injury Induced by Intensity-modulated Radiotherapy in Patients with Esophageal Cancer*

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ABSTRACT Objective: To analyze the risk factors of radioactive lung injury induced by intensity-modulated radiotherapy in patients with esophageal cancer. **Methods:** A total of 100 patients with esophageal cancer, who received intensity-modulated radiotherapy in the Affiliated Hospital of Qinghai Medical College from February 2015 to February 2018, were selected as research subjects. The data such as age, sex, smoking history, synchronous chemotherapy, karnofsky, tumor stage and radiation dosimetry factors V5, V10, V20, V30, and Dmean situation were collected. Univariate and multivariate Logistic regression analysis were used to analyze the risk factors of radioactive lung injury induced by intensity-modulated radiotherapy in patients with esophageal cancer. **Results:** Among the 100 patients, there were 27 cases of radioactive lung injury, the incidence was 27.00%, in which, there were 20 cases at grade 1 and 7 cases at grade 2. Univariate analysis showed that radioactive lung injury induced by intensity-modulated radiotherapy in patients with esophageal cancer were related to karnofsk, V5, V10, V20, V30 and Dmean ($P<0.05$), but not related to sex, age, smoking history, synchronous chemotherapy and tumor stage ($P>0.05$). Multivariate logistic regression analysis showed that karnofsk <80 scores, $V5>60\%$, $V10>40\%$, $V20>25\%$, $V30>20\%$, and $Dmean >10\%$ were the independent risk factors of radioactive lung injury induced by intensity-modulated radiotherapy in patients with esophageal cancer ($P<0.05$). **Conclusion:** The incidence of radioactive lung injury induced by intensity-modulated radiotherapy in patients with esophageal cancer is higher. And it is closely related to karnofsk and radiation dosimetry factors such as V5, V10, V20, V30 and Dmean. In clinical work, the risk of radioactive lung injury can be reduced by controlling the dose of lung tissue.

Key words: Esophageal cancer; Intensity-modulated radiotherapy; Radioactive lung injury; Risk factors

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前言

近年来,随着医疗水平的不断进步以及放疗技术的逐渐完善,调强放疗作为一种治疗恶性肿瘤的有效手段开始被广泛应用于临床多种恶性肿瘤中^[1,2]。该治疗方式主要是在充分保护患者重要器官的基础上,对肿瘤靶区进行精准照射,从而达到杀伤肿瘤细胞、促进患者康复的目的^[3,4]。然而,患者在接受调强放疗后易并发放射性肺损伤,从而会对放疗疗效产生一定程度的影响,同时会降低患者的生活质量,严重时甚至可导致患者死亡^[5]。食管癌是临床较为常见的消化系统恶性肿瘤之一,具有发病率高、病死率高的特点^[6,7]。目前,临床上治疗食管癌主要以手术为主,然而由于食管癌的解剖结构较为特殊,因此手术难度较大,无法通过手术将恶性肿瘤彻底清扫,绝大部分患者在术后均需采用放化疗进行辅助治疗,而调强放疗是临床食管癌患者术后应用最为广泛的辅助治疗手段之一^[8-10]。鉴于此,本文通过研究食管癌调强放疗并发放射性肺损伤的危险因素,旨在为防治食管癌患者调强放疗并发放射性肺损伤提供参考依据,现作以下报道。

1 资料与方法

1.1 一般资料

以 2015 年 2 月 -2018 年 2 月于青海医学院附属医院接受调强放疗的食管癌患者 100 例为研究对象。纳入标准:(1)所有患者均经手术病理组织活检以及影像学检查确诊为食管癌,并于本院接受调强放疗者;(2)卡氏评分 ≥ 70 分;(3)临床病历资料完整者;(4)均为首次接受放疗者。排除标准:(1)存在放、化疗禁忌症者;(2)合并严重心、肾功能障碍者;(3)合并其他恶性肿瘤者;(4)合并精神疾病或交流沟通障碍者。其中男性患者 62 例,女性患者 38 例,年龄 41-78 岁,平均 (62.31 ± 6.23) 岁;有吸烟史者 60 例,无吸烟史者 40 例;接受同步化疗者 17 例,未接受同步化疗者 83 例;卡氏评分 <80 分 58 例, ≥ 80 分 42 例;肿瘤分期:T1-T2 期 47 例,T3-T4 期 53 例;放射剂量学因素:V5 $<60\%$ 52 例,V5 $\geq 60\%$ 48 例;V10 $<40\%$ 50 例,V10 $\geq 40\%$ 50 例;V20 $<25\%$ 67 例,V20 $\geq 25\%$ 33 例;V30 $<20\%$ 76 例,V30 $\geq 20\%$ 24 例;平均剂量(Dmean) $<10\text{Gy}$ 47 例,Dmean $\geq 10\text{Gy}$ 53 例。所有患者均签署了知情同意书,我院伦理委员会已批准此次研究。

1.2 研究方法

(1)调强放疗:所有患者均予以螺旋 CT 模拟定位,层厚为 0.5cm,扫描范围自下颌骨下缘直至肝下缘,并将扫描图像传输至 Eclipse8.6 治疗计划系统,由专业医师完成靶区以及危及器官的勾画。正常组织剂量如下:肺平均剂量 $\leq 13\text{Gy}$,双肺 V20 $\leq 30\%$,脊髓剂量 $\leq 40-45\text{Gy}$,心脏 30%体积对应的剂量 $\leq 40\text{Gy}$,心脏 40%体积对应的剂量 $\leq 30\text{Gy}$ 。(2)其中 17 例患者接受同步化疗:方案为紫杉醇(Hospira Australia Pty Ltd,批准文号:H20090175)+顺铂(贵州汉方制药有限公司,国药准字:H20020272),其中紫杉醇 135-175 mg/m^2 ,d1;顺铂 20 mg/m^2 ,d1-d4;以 21d 为一个疗程,连续化疗 4 个疗程。(3)分别收集患者年龄、性别、吸烟史、同步化疗情况、卡氏评分、肿瘤分期等资料以及放射剂量学因素 V5、V10、V20、V30、Dmean 情况。其中

V5、V10、V20、V30 分别指双侧肺接受 5Gy、10Gy、20Gy、30Gy 照射剂量的肺体积占全肺体积的百分比。

1.3 评价标准

放射性肺损伤判定标准如下^[11]:严格按照美国放射治疗协作组所制定的相关标准对患者进行分级:轻微咳嗽或劳累时存在呼吸困难即为 1 级;存在持续性咳嗽,轻微用力即出现呼吸困难,需予以麻醉药止咳即为 2 级;存在严重咳嗽,使用麻醉药止咳无缓解,且经临床以及影像学检查确诊为急性肺损伤,需予以吸氧或激素治疗即为 3 级;呼吸苦难,需持续吸氧或辅助通气即为 4 级。

1.4 统计学方法

本研究数据均采用 SPSS20.0 软件进行统计分析,采用[n(%)]表示计数资料,实施 χ^2 检验。食管癌调强放疗患者并发放射性肺损伤的危险因素予以多因素 Logistic 回归分析。 $P<0.05$ 表明两组数据对比差异具有统计学意义。

2 结果

2.1 所有患者放射性肺损伤发生情况分析

100 例患者发生放射性肺损伤人数为 27 例,发生率为 27.00%。其中 1 级 20 例,2 级 7 例,3 级 0 例,4 级 0 例。

2.2 食管癌调强放疗并发放射性肺损伤的单因素分析

经单因素分析可得:食管癌调强放疗并发放射性肺损伤与卡氏评分、V5、V10、V20、V30 以及 Dmean 有关($P<0.05$);与性别、年龄、吸烟史、同步化疗、肿瘤分期无关($P>0.05$)。见表 1。

2.3 食管癌调强放疗患者并发放射性肺损伤的多因素 Logistic 回归分析

经多因素 Logistic 回归分析可得:卡氏评分 <80 分、V5 $\geq 60\%$ 、V10 $\geq 40\%$ 、V20 $\geq 25\%$ 、V30 $\geq 20\%$ 、Dmean $\geq 10\%$ 均是食管癌调强放疗患者并发放射性肺损伤的独立危险因素($P<0.05$),见表 2。

3 讨论

食管癌是我国发病率以及死亡率较高的消化道恶性肿瘤之一,由于该病患者在发病早期存在较强的隐匿性,因此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,放疗、化疗成为该病患者最常用的治疗手段^[12,13]。有研究报道显示,肺部属于放射敏感脏器之一,因此接受放疗患者存在并发放射性肺损伤的风险^[14,15]。放射性肺损伤患者主要临床症状表现为胸闷、胸痛、发热、干咳以及气短等,病情严重者甚至会出现呼吸衰竭,从而对放射治疗剂量的提升造成一定的限制,导致患者治疗不彻底,不利于预后^[16-18]。另有研究报道表明,放射性肺损伤是一个十分复杂的过程,多种细胞因子与分子的相互作用在其中发挥着至关重要的作用^[19-21]。目前,放射性肺损伤已成为严重影响食管癌患者近期疗效以及长期生活质量的主要因素,引起了医务人员的广泛关注。此外,由于放射性肺损伤的具体发生机制尚未完全明确,其预测难度较大,且放射性肺损伤的发生通常具有滞后性,因此如何有效预测和预防放射性肺损伤显得尤为重要。

本研究结果发现,100 例患者中发生放射性肺损伤人数为 27 例,发生率为 27.00%。而孟令新等人^[22]通过研究食管癌术后

表 1 食管癌调强放疗并发放射性肺损伤的单因素分析[n(%)]

Table 1 Univariate analysis of radioactive lung injury induced by intensity-modulated radiotherapy in patients with esophageal cancer[n(%)]

Factors		n	Incidence of radioactive lung injury	χ^2	P
Sex	Male	62	16(25.81)	0.118	0.731
	Female	38	11(28.95)		
Age(years old)	<60	31	9(29.03)	0.094	0.760
	≥ 60	69	18(26.09)		
Smoking history	Yes	60	17(28.33)	0.135	0.713
	No	40	10(25.00)		
Synchronous chemotherapy	Yes	17	4(23.53)	0.125	0.723
	No	83	23(27.71)		
Karnofsky(score)	<80	58	20(34.48)	3.923	0.048
	≥ 80	42	7(16.67)		
Tumor stage	T1-T2 stage	47	12(25.53)	0.097	0.755
	T3-T4 stage	53	15(28.30)		
V5(%)	<60	52	6(11.54)	13.140	0.000
	≥ 60	48	21(43.75)		
V10(%)	<40	50	9(18.00)	4.110	0.043
	≥ 40	50	18(36.00)		
V20(%)	<25	67	11(16.42)	11.535	0.001
	≥ 25	33	16(48.48)		
V30(%)	<20	76	15(19.74)	8.476	0.004
	≥ 20	24	12(50.00)		
Dmean(Gy)	<10	47	7(14.89)	6.594	0.010
	≥ 10	53	20(37.74)		

表 2 食管癌调强放疗患者并发放射性肺损伤的多因素 Logistic 回归分析

Table 2 Multivariate Logistic regression analysis of radioactive lung injury induced by intensity-modulated radiotherapy in patients with esophageal cancer

Indexes	β	SE	Wald χ^2	P	OR	95%CI
Karnofsky <80 scores	1.114	2.953	3.982	0.017	1.543	0.341-1.754
V5≥ 60%	3.241	3.448	4.006	0.001	1.830	0.746-2.366
V10≥ 40%	5.038	5.035	4.027	0.000	3.425	1.349-8.590
V20≥ 25%	2.415	2.562	3.651	0.026	2.586	0.396-4.865
V30≥ 20%	2.857	3.859	5.258	0.000	1.584	1.053-5.932
Dmean≥ 10Gy	3.075	4.018	5.241	0.000	1.753	1.185-4.381

患者在调强放疗中导致放射性肺损伤的相关因素中发现,65例食管癌切除术患者并发放射性肺损伤的发生率为26.2%,与本研究结果存在高度一致性。提示了在临床工作中应重点关注食管癌调强放疗患者并发放射性肺损伤情况,从而为改善患者预后提供参考依据。此外,经单因素分析可得:食管癌调强放疗并发放射性肺损伤与卡氏评分、V5、V10、V20、V30以及Dmean有关。随着卡氏评分的不断增加,患者并发放射性肺损伤的风险越低;与此同时,放射剂量与食管癌患者调强放疗并发放射性肺损伤密切相关,且随着放射剂量的增加,放射性肺

损伤风险越大^[23-25]。分析原因,我们认为卡氏评分主要是用以反映机体功能状态的指标,且得分越高表示患者健康状况越佳,能更好地耐受化疗对身体造成的副作用,从而得到更为彻底的治疗,降低放射性肺损伤发生风险^[26,27]。而放射剂量与放射性肺损伤关系可能与照射区域所覆盖的肺组织对放射性肺损伤有直接影响有关^[28,29]。宋永浩等^[30]人的报道指出,调强适形放疗所导致的老年食管癌放射性肺损伤具有较多的影响因素,这也值得临床加以关注。本研究经多因素 Logistic 回归分析可得:卡氏评分 <80 分、V5≥ 60%、V10≥ 40%、V20≥ 25%、V30≥ 20%、

Dmean $\geq$ 10%均是食管癌调强放疗患者并发放射性肺损伤的独立危险因素。这充分证明了上述结果,提示了在临床工作中应针对上述各项因素制定相关干预措施,以达到降低放射性肺损伤发生的风险,从而改善患者预后。值得一提的是,此次研究尚且存在样本量不足等缺陷,也缺乏了多级医疗机构的协同性研究,因此在今后的研究中可尝试增大样本量,以获取更为准确的数据结论。

综上所述,卡氏评分以及放射剂量学因素 V5、V10、V20、V30、Dmean 与食管癌调强放疗并发放射性肺损伤关系密切,临床工作中可通过改善患者卡氏评分以及减少放射剂量等途径,达到降低放射性并发症发生的目的。

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