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Impacts of hyperfractionated radiotherapy at different fractionated doses on short- and long-term efficacy and toxicity in patients with limited stage small cell lung cancer

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Abstract: Objective To explore the short- and long-term efficacy and toxic and side effects of hyperfractionated radiotherapy with different fractionation doses in patients with limited stage small cell lung cancer (SCLC). **Methods** From August 2017 to August 2019, 70 patients with limited-stage SCLC admitted to Zhangye People's Hospital were selected and divided into control group (n=35) and observation group (n=35) according to the random number table method. Conventional chemotherapy and hyperfractionated radiotherapy were used in both groups, with a total dose of 45 Gy in the control group and 60 Gy in the observation group. A three-year follow-up was carried out to compare the short- and long-term efficacy (survival and local control rate), and the occurrence of toxic side effects between the two groups. **Results** The total effective rate in the observation group was obviously higher than that in the control group (91.43% *vs* 71.43%, χ^2=4.629, P=0.031). The 1-, 2-, and 3-year local control rates and survival rates of patients in the observation group were significantly higher than those in the control group (P<0.05). There was no statistically significant difference in the total incidence of adverse reactions between the two groups (P>0.05), and most of adverse reactions were grade Ⅰ-Ⅱ, which did not affect the course of treatment. After treatment, the scores of life quality in both groups increased significantly (P<0.05), and the observation group showed a significant increase compared to the control group (P<0.05). **Conclusion** Hyperfractionnated radiotherapy with appropriately increased fractionated dose for patients with limited-stage SCLC has better short- and long-term efficacy, higher local control rate and survival, and no significant increase in toxic and side effects, which is safe and can improve the quality of patients' life.

Keywords: Hyperfractionated radiotherapy; Limited stage; Small cell lung cancer; Efficacy, short-term, long-term; Toxic and side effects

Lung cancer is a common malignant tumor. In 2020, China had the largest number of new lung cancer cases in the world [1]. Lung cancer is mainly divided into small cell lung cancer (SCLC) and non-small cell lung cancer [2]. SCLC is a highly invasive neuroendocrine tumor, accounting for about 15% of lung cancer patients. Due to the rapid proliferation of cancer cells, rapid development and high malignancy of SCLC, about 70% patients were diagnosed as extensive SCLC, and only about 30% were diagnosed as localized SCLC, but its prognosis is still poor [3-4]. Radiotherapy includes oncology, radiobiology, clinical radiotherapy, radiation physics and other technologies, which have good therapeutic effects on many malignant tumors. Because SCLC is sensitive to chemotherapy and radiotherapy, limited-stage SCLC is mainly treated by radiotherapy combined with chemotherapy [5]. In radiotherapy, most of them use fractionated radiotherapy. With the development of technology, some studies have shown that hyperfractionated radiotherapy is superior to conventional fractionated radiotherapy [6]. At present, there are few reports on the short-term and long-term efficacy and side effects of different fractionated doses. Moreover, there is no uniform standard for the optimal dose in the concurrent chemoradiotherapy regimen of limited-stage SCLC, and different fractionated doses will increase the toxicity and side effects of treatment. Therefore, the aim of this study is to investigate the effects of hyperfractionated radiotherapy at different fractionated doses on the short-term and long-term efficacy and toxicity of patients with limited-stage SCLC.

1. Materials and Methods

1.1 General information

Seventy patients with limited-stage SCLC who were admitted to Zhangye People's Hospital Affiliated to Hexi University from August 2017 to August 2019 were

selected, including 44 males and 26 females.

Inclusion criteria:

(1) limited-stage SCLC was confirmed by pathological examination;

(2) having an indication for the treatment regimen used in the study;

(3) good compliance;

(4) complete clinical data;

(5) Patients voluntarily enrolled in the study and signed the informed consent.

Exclusion criteria:

(1) contraindications to radiotherapy and chemotherapy;

(2) patients with a history of myocardial infarction;

(3) patients with severe liver and kidney dysfunction;

(4) patients with a chemotherapy history;

(5) those who gave up treatment.

All patients were divided into two groups by a random number table method. The control group (n=35), 21 males and 14 females; The average age was (54.82±9.56) years. The maximum diameter of tumor was (3.18±1.01) cm. There were 17 cases of central type and 18 cases of peripheral type. The observation group (n=35), 23 males and 12 females; The average age was (55.48±9.37) years old. The maximum diameter of tumor was (3.11±0.98) cm. There were 19 cases of central type and 16 cases of peripheral type. There was no significant difference in basic data between the two groups (P>0.05). This study was approved by the ethics committee of our hospital (2017-06201).

1.2 Treatment Methods

Conventional chemotherapy and hyperfractionated radiotherapy were used in both groups. Conventional chemotherapy: 100 mg/m^2 etoposide, day 1-5; 80 mg/m^2 cisplatin, day 1-3. Concurrent radiotherapy was performed after one cycle of chemotherapy (3 weeks), and chemotherapy was continued for 4 cycles. Hyperfractionated radiotherapy: a linear accelerator was used and a vacuum bag was used to fix the patient's lesions for operation. Enhanced CT simulation positioning was performed with a thickness of 5 mm, and the patient needed to breathe smoothly. The scanning was performed from the thoracic inlet to the horizontal plane of the costophrenic angle, and the three-dimensional image was reconstructed according to the returned image. The target volume was determined by discussion between oncologists and radiologists, the position of lesions was determined through the lung window, and the position of lymph nodes was determined through the mediastinal window. The clinical target volume was defined according to the range of lymph nodes and the range of tumors before chemotherapy. The planning target volume was defined according to the setup error and respiratory activity. Patients were given chest X-ray examination once a week, and the treatment target volume was adjusted according to the condition before treatment.

The total dose of radiotherapy in the control group and the observation group was 45 Gy and 60 Gy, 1.5 Gy each time, 2 times a day, no more than 5 times a week, a total of 4 cycles of radiotherapy.

1.3 Observation indicators

1.3.1 Short-term efficacy

After the treatment, the efficacy of all patients was evaluated (no dropout).

Complete remission: the clinical symptoms and imaging examination of the tumor disappeared, and lasted for more than 30 days.

Partial response: the clinical symptoms were relieved, the tumor diameter decreased by more than 50%, and no new lesions appeared for more than 30 days.

Stable disease: the tumor was reduced by 25%-50% on imaging examination, and no new lesions appeared.

Disease progression: appearance of new lesions or tumor enlargement by 25%.

Total effective rate = (complete remission + partial remission)/ total number of patients ×100% [7].

1.3.2 Long-term efficacy

All patients were followed up for 3 years, mainly by telephone follow-up and regular review (no dropout). The survival rate and local control rate within 1, 2 and 3 years were statistically analyzed and compared between the two groups.

1.3.3 Toxic and side effects

During the treatment period, patients with toxic and side effects were checked once a week for routine blood tests, and the occurrence of adverse reactions was recorded to judge the toxic and side effects. According to the standard of WHO toxic and side effects, they were divided into grades I-IV [8].

1.3.4 Quality of life

Patients were evaluated by quality-of-life scale before and after 1 month of treatment, mainly including mental and physiological function, etc. The full score was 100 points, and the higher the score, the better the quality of life [9].

1.4 Statistical methods

The data were analyzed by SPSS 25.0 software. Count data were expressed as case (%) and compared by test. Measurement data with non-normal distribution were represented as $M(P_{25}, P_{75})$, and Mann-Whitney U test was used for comparison between and within groups. P<0.05 was considered statistically significant.

2 Results

2.1 Comparison of short-term efficacy between the two groups

The total effective rate of the observation group

was significantly better than that of the control group, and the difference was significant (P<0.05). [Table 1]

2.2 Comparison of local control rate and survival rate between the two groups in each year

The 1 -, 2 -, and 3-year local control rate and survival rate of the observation group were significantly higher than those of the control group (P < 0.05). See Table 2.

2.3 Comparison of adverse reactions between the two groups

Most of the adverse reactions in the two groups were grade I-II, which did not affect the treatment course. There was no significant difference in the total incidence of nausea and vomiting, abnormal liver function, abnormal renal function, pneumonia, and leukopenia between the observation group and the control group (P>0.05). See Table 3.

2.4 Comparison of quality-of-life scores between the two groups before and after treatment

There was no significant difference in the quality-of-life scores between the two groups before treatment (P>0.05). After treatment, the quality-of-life scores in the two groups were significantly increased (P<0.01), and the quality-of-life score in the observation group was significantly higher than that in the control group (P<0.01). See Table 4.

Tab. 1 Comparison of recent therapeutic effects between two groups of patients [n=35, case (%)]

Group	Complete remission	Partial response	Stable disease	Disease Progression	Total Effective Rate
Observation Group	12(34.28)	20(57.14)	2(5.71)	1(2.86)	32(91.43)
Control Group	8(22.86)	17(48.57)	7(20.00)	3(8.57)	25(71.43)
χ^2 value					4.629
***P* value**					0.031

Tab.2 Comparison of local control rates and survival within 3 years between two groups of patients [n=35, case (%)]

Group	Local Control Rates			Survival Rates		
	1 year	2 years	3 years	1 year	2 years	3 years
Observation Group	29(82.86)	27(77.14)	25(71.43)	30(85.71)	24(68.57)	19(54.29)
Control Group	21(60.00)	19(54.29)	16(45.71)	22(62.86)	15(42.86)	10(28.57)
χ^2 value	4.480	4.058	4.769	4.786	4.690	4.769
***P* value**	0.034	0.044	0.029	0.029	0.030	0.029

Tab.3 Comparison of toxic and side effects between two groups of patients [n=35, case (%)]

Group		Nausea and Vomiting	Abnormal Liver Function	Abnormal Renal Function	Pneumonia	Leukopenia
Observation Group	I-II	15(42.86)	18(31.43)	21(60.00)	18(51.42)	21(60.00)
	III-IV	0	1(2.86)	0	1(2.86)	2(5.71)
	Total	15(42.86)	19(54.28)	21(60.00)	19(54.28)	23(65.71)
Control Group	I-II	16(45.71)	18(51.43)	18(51.43)	17(48.57)	18(51.43)
	III-IV	1(2.86)	0	0	0	1(2.86)
	Total	17(48.57)	18(51.43)	18(51.43)	17(48.57)	19(54.29)
χ^2 value[a]		0.230	0.057	0.521	0.229	0.952
***P* value[a]**		0.631	0.811	0.47	0.632	0.329

Note: Compared with the group before treatment, [a]P<0.01

Tab.4 Comparison of quality of life scores between two groups of patients before and after treatment [n=35, $M(P_{25},P_{75})$]

Group	Before treatment	After treatment	*Z* value	*P* value
Observation Group	36.00(34.00,40.00)	80.00(77.00,82.00)	7.205	<0.001
Control Group	37.00(34.00,38.00)	59.00(57.00,61.00)	7.207	<0.001
***Z* value**	0.195	7.205		
***P* value**	0.846	<0.001		

3 Discussion

SCLC is a common malignant disease in respiratory medicine, accounting for about 15% of lung cancer. It has the characteristics of rapid spread, rapid growth and a high degree of malignancy. The main manifestations are sputum blood, cough, fever, chest pain, hoarseness and so on. At present, the pathogenesis and etiology of SCLC is still unknown and may be due to the damage of epithelial cells by carcinogen [10-11]. Although the drugs and methods for treating lung cancer have developed rapidly, the 5-year survival rate of lung cancer patients is still relatively low, and their mortality ranks first among malignant tumors in China [12-13].

Chemotherapy is a systemic treatment, while radiotherapy is a local treatment. Studies have shown that chemotherapy combined with radiotherapy can work together to achieve the purpose of improving efficacy [14]. Limited-stage SCLC is mainly treated with radiotherapy and chemotherapy. Theoretically, increasing the radiotherapy dose is more conducive to killing tumor cells. Studies have shown that the increase of radiotherapy dose will enhance the killing of tumors and improve the treatment effect [15]. Other studies have found that with the increase of radiotherapy dose, the toxic side effects and corresponding risks also increase [16]. In this study, both groups of patients were treated with hyperfractionated radiotherapy on the basis of conventional chemotherapy, and the difference was that the radiation dose of the observation group was appropriately increased. The results showed that the total effective rate of the observation group was significantly better than that of the control group. Although the two groups of patients had toxic side effects, most of them were grade I-II, which did not affect the course of treatment, and the total incidence of toxic side effects between the two groups was small. It is suggested that increasing the radiation dose appropriately can improve the clinical efficacy without increasing the risk of side effects, and the safety is good.

In this study, all patients with limited-stage SCLC were treated with hyperfractionated radiotherapy, and the tumor cells did not metastasize or spread. Due to the rapid reproduction rate of lung cancer cells, studies have shown that the survival rate of patients will be reduced by about 2% for every day of treatment delay [17]. Hyperfractionated therapy can reduce the total treatment time, thereby reducing the risk of lung cancer cell proliferation and improving the survival rate of patients [18]. The results of this study showed that compared with the control group, the control rate and survival rate of 1, 2 and 3 years in the observation group were significantly higher. The quality-of-life scores of the two groups were significantly increased after treatment, and the observation group was significantly higher than the control group, suggesting that appropriately increasing the dose can effectively inhibit the proliferation of lung cancer cells, improve the curative effect, survival rate and quality of life of patients. Studies have found that an appropriate increase in radiotherapy dose can enhance the efficacy of locally advanced non-small cell carcinoma without increasing toxic and side effects, with high safety [19-20]. The results of the present study were similar.

In conclusion, hyperfractionated radiotherapy in the treatment of LS-SCLC has better short-term and long-term efficacy, better control rate and survival rate, and does not increase the toxic side effects. It is safe and can improve the quality of life of patients. However, this study also has certain limitations. The selected sample size is small, which may lead to a certain bias in the results of the study.

Conflict of Interest None

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·论　著·

不同分割剂量超分割放疗对局限期小细胞肺癌患者近远期疗效及毒副反应的影响

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摘要：目的　探讨对局限期小细胞肺癌(SCLC)患者采用不同分割剂量超分割放疗治疗的近远期疗效及毒副反应。**方法**　选取 2017 年 8 月至 2019 年 8 月在张掖人民医院收治的局限期 SCLC 患者 70 例,按照随机数字表法分为对照组(n=35)和观察组(n=35),两组患者都采用常规化疗和超分割放疗,对照组放疗的总剂量是 45 Gy,观察组放疗的总剂量是 60 Gy。进行为期 3 年的随访,比较两组患者的近期疗效、远期疗效(生存率和局部控制率)、毒副反应的发生情况。**结果**　观察组患者总有效率优于对照组(91.43% *vs* 71.43%,χ^2=4.629, P=0.031);观察组患者 1、2、3 年的局部控制率和生存率高于对照组(P<0.05)。两组不良反应总发生率差异无统计学意义(P>0.05),且不良反应多为Ⅰ~Ⅱ级,不影响疗程。两组生活质量评分在治疗后均升高(P<0.01),且观察组高于对照组(P<0.01)。**结论**　超分割放疗治疗局限期 SCLC 患者,适当加大分割剂量,则近远期疗效更好,局部控制率和生存率更高,且毒副反应未明显增多,安全性较好,可以提高患者的生活质量。

关键词： 超分割放疗；局限期；小细胞肺癌；疗效，近期，远期；毒副反应

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Impacts of hyperfractionated radiotherapy at different fractionated doses on short- and long-term efficacy and toxicity in patients with limited stage small cell lung cancer

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Abstract: Objective　To explore the short- and long-term efficacy and toxic and side effects of hyperfractionated radiotherapy with different fractionated doses in patients with limited stage small cell lung cancer (SCLC). **Methods**　From August 2017 to August 2019, 70 patients with limited stage SCLC admitted to Zhangye People's Hospital were selected and divided into control group (n=35) and observation group (n=35) according to the random number table method. Conventional chemotherapy and hyperfractionated radiotherapy were used in both groups, with a total dose of 45 Gy in the control group and 60 Gy in the observation group. A three-year follow-up was carried out to compare the short- and long-term efficacy (survival and local control rate), and the occurrence of toxic and side effects between the two groups. **Results**　The total effective rate in the observation group was obviously higher than that in the control group (91.43% *vs* 71.43%, χ^2=4.629, P=0.031). The 1-, 2-, and 3-year local control rates and survival rates of patients in the observation group were significantly higher than those in the control group (P<0.05). There was no statistically significant difference in the total incidence of adverse reactions between the two groups (P>0.05), and most of adverse reactions were grade Ⅰ-Ⅱ, which did not affect the course of treatment. After treatment, the scores of life quality in

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both groups increased significantly ($P<0.01$), and the observation group showed a significant increase compared to the control group ($P<0.01$). **Conclusion**　Hyperfractionnated radiotherapy with appropriately increased fractionated dose for patients with limited stage SCLC has better short- and long-term efficacy, higher local control rate and survival, and no significant increase in toxic and side effects, which is safe and can improve the quality of patients' life.

Keywords: Hyperfractionated radiotherapy; Limited stage; Small cell lung cancer; Efficacy, short-term, long-term; Toxic and side effects

Fund program: Gansu Province Health Industry Research Project (GSWSKY2021-057); Lanzhou Talent Innovation and Entrepreneurship Project (2021-RC-130)

肺癌是一种常见的恶性肿瘤,2020 年,我国是全球当年新发肺癌病例最多的国家[1]。肺癌主要分为小细胞肺癌(small cell lung cancer, SCLC)和非小细胞肺癌[2],SCLC 是一种具有较高侵袭性的神经内分泌肿瘤,约占肺癌患者的 15%,由于 SCLC 发展快、癌细胞增殖快、恶性度高的特点,约 70%被诊断为广泛性 SCLC,只有约 30%被诊断为局限期 SCLC,但其预后仍不容乐观[3-4]。放疗包括肿瘤学、放射生物、临床放疗、放射物理等技术,对许多恶性肿瘤都有良好的治疗效果,由于 SCLC 对化疗和放疗敏感,所以局限期 SCLC 主要通过放疗联合化疗的方式进行治疗[5]。放疗时,大多数采取分割放疗的方式,随着技术的发展,有研究表示超分割放疗优于常规分割放疗[6]。目前关于不同分割剂量的近远期疗效及毒副反应的研究鲜有报道,而且局限期 SCLC 同步放化疗的方案中对最佳剂量尚无统一标准,不同分割剂量会使治疗毒性不良反应增加,对此尚无统一的结论,因此本研究探讨不同分割剂量超分割放疗对局限期 SCLC 患者近远期疗效及毒副反应的影响。

1　资料与方法

1.1　一般资料　于 2017 年 8 月至 2019 年 8 月选取在河西学院附属张掖人民医院收治的局限期 SCLC 患者 70 例,其中男性 44 例,女性 26 例。纳入标准:(1) 经病理检查确诊为局限期 SCLC;(2) 具有本研究使用的治疗方案的适应证;(3) 依从性良好;(4) 临床资料完整;(5) 自愿入组并签署了知情同意书。排除标准:(1) 放化疗禁忌证者;(2) 合并心肌梗死史者;(3) 合并严重肝肾功能障碍者;(4) 有化疗史者;(5) 放弃治疗者。将所有患者按随机数字表法分为两组。对照组($n=35$),男 21 例,女 14 例;年龄(54.82±9.56)岁;肿瘤最大直径为(3.18±1.01)cm;中央型 17 例,周围型 18 例。观察组($n=35$),男 23 例,女 12 例;年龄(55.48±9.37)岁;肿瘤最大直径为(3.11±0.98)cm;中央型 19 例,周围型 16 例。两组基本资料比较差异无统计学意义($P>0.05$)。本研究经医院伦理委员会审核批准(2017-06201)。

1.2　治疗方法　两组均采用常规化疗和超分割放疗。常规化疗:100 mg/m^2 依托泊苷,第 1~5 天;80 mg/m^{2}顺铂,第 1~3 天,治疗 5 d,间歇 16 d, 3 周为 1 个周期。同步放疗于化疗 1 个周期后进行,并继续化疗至 4 个周期。超分割放疗:采用直线加速器,真空袋固定患者的病灶进行操作。采用强化 CT 模拟定位,患者保持平稳呼吸,扫描厚度为 5 mm,从胸廓入口至肋膈角水平面范围进行扫描,根据回传图像重建三维影像。由肿瘤和放射科的医生讨论画出靶区,通过肺窗确定病灶的位置,通过纵隔窗确定淋巴结的位置,根据淋巴结的范围和化疗前肿瘤范围划定临床靶体积,根据摆位误差和呼吸活动度划定计划靶区,同时结合临床操作,确定照射野的分次和权重值。患者每周给予 1 次 X 线胸片检查,根据治疗前病情来调整治疗靶区。

对照组和观察组放疗的总剂量分别是 45 Gy 和 60 Gy,每次 1.5 Gy,每天治疗 2 次,每周不能超过 5 次,总共放疗 4 个周期。

1.3　观察指标

1.3.1　近期疗效　治疗结束后对所有患者的疗效进行评估(无中途退出者)。完全缓解:临床症状和影像检查肿瘤基本消失,并持续 30 d 以上;部分缓解:临床症状减轻,影像检查肿瘤变小,肿瘤直径缩小超过 50%,持续 30 d 以上没有新病变出现;病情稳定:影像检查肿瘤变小 25%~50%,没有出现新病变;病情进展:出现新病变或肿瘤增大 25%。总有效率=(完全缓解+部分缓解)例数/本组例数×100%[7]。

1.3.2　远期疗效　对患者随访 3 年,主要以电话随访和定期复查的方式(无中途退出者),统计两组患者 1、2、3 年内的生存率和局部控制率并比较。

1.3.3　毒副反应　患者在治疗期间,每周检查 1 次血常规,且记录患者不良反应的发生情况,从而判断毒副作用,按 WHO 毒副反应的标准进行评定,分为Ⅰ~Ⅳ级[8]。

1.3.4　生活质量　在治疗前和治疗 1 个月后采用生活质量量表对患者生活质量进行评估,主要包括精神、生理功能等,满分为 100 分,得分越高,说明生活质量越好[9]。

1.4　统计学方法　本研究数据采用 SPSS 25.0 软件分析。计数资料以例(%)表示,比较采用χ^2 检验;非正态分布的计量资料以 $M(P_{25},P_{75})$ 表示,组间和组内比较均采用 Mann-Whitney U 检验。$P<0.05$ 为差异有统计学意义。

2　结　果

2.1　两组患者近期疗效的比较　两组患者全部完成放化疗疗程,无中途退出者。观察组患者总有效率优于对照组,差异有统计学意义($P<0.05$)。见表 1。

2.2　两组患者各年局部控制率和生存率的比较　观察组患者 1、2、3 年的局部控制率和生存率均高于对照组($P<0.05$)。见表 2。

2.3　两组患者毒副反应的比较　两组患者的不良反应多数为Ⅰ~Ⅱ级,不影响疗程。观察组患者的恶心呕吐、肝功能异常、肾功能异常、肺炎、白细胞下降的总发生率与对照组相比差异无统计学意义($P>0.05$)。见表 3。

2.4　两组患者治疗前后生活质量评分的比较　两组生活质量评分治疗前比较差异无统计学意义($P>0.05$),治疗后两组均显著升高($P<0.01$),且观察组显著高于对照组($P<0.01$)。见表 4。

表 1　两组患者近期疗效的比较　[$n=35$, 例(%)]

Tab. 1　Comparison of recent therapeutic effects between two groups of patients　[$n=35$, case(%)]

组别	完全缓解	部分缓解	病情稳定	病情进展	总有效
观察组	12(34.28)	20(57.14)	2(5.71)	1(2.86)	32(91.43)
对照组	8(22.86)	17(48.57)	7(20.00)	3(8.57)	25(71.43)
χ^2 值					4.629
P 值					0.031

表 2　两组患者 3 年内局部控制率和生存率的比较　[$n=35$, 例(%)]

Tab. 2　Comparison of local control rates and survival within 3 years between two groups of patients　[$n=35$, case(%)]

组别	指标	1 年	2 年	3 年
观察组	局部控制率	29(82.86)	27(77.14)	25(71.43)
对照组	局部控制率	21(60.00)	19(54.29)	16(45.71)
χ^2 值		4.480	4.058	4.769
P 值		0.034	0.044	0.029
观察组	生存率	30(85.71)	24(68.57)	19(54.29)
对照组	生存率	22(62.86)	15(42.86)	10(28.57)
χ^2 值		4.786	4.690	4.769
P 值		0.029	0.030	0.029

表 3　两组患者毒副反应的比较　[$n=35$, 例(%)]

Tab. 3　Comparison of toxic and side effects between two groups of patients　[$n=35$, case(%)]

组别	分级	恶心呕吐	肝功能异常	肾功能异常	肺炎	白细胞下降
观察组	Ⅰ~Ⅱ	15(42.86)	18(31.43)	21(60.00)	18(51.42)	21(60.00)
	Ⅲ~Ⅳ	0	1(2.86)	0	1(2.86)	2(5.71)
	总发生	15(42.86)	19(54.28)	21(60.00)	19(54.28)	23(65.71)
对照组	Ⅰ~Ⅱ	16(45.71)	18(51.43)	18(51.43)	17(48.57)	18(51.43)
	Ⅲ~Ⅳ	1(2.86)	0	0	0	1(2.86)
	总发生	17(48.57)	18(51.43)	18(51.43)	17(48.57)	19(54.29)
χ^2 值[a]		0.230	0.057	0.521	0.229	0.952
P 值[a]		0.631	0.811	0.470	0.632	0.329

注:[a] 表示两组总发生率的比较。

表 4　两组患者治疗前后生活质量评分的比较　[$M(P_{25},P_{75})$]

Tab. 4　Comparison of life quality scores between two groups of patients before and after treatment　[$M(P_{25},P_{75})$]

组别	例数	治疗前	治疗后
观察组	35	36.00(34.00,40.00)	80.00(77.00,82.00)[a]
对照组	35	37.00(34.00,38.00)	59.00(57.00,61.00)[a]
Z 值		0.195	7.205
P 值		0.846	<0.001

注:与本组治疗前比较,[a]$P<0.01$。

3　讨　论

SCLC 是一种常见的呼吸内科恶性疾病,在肺癌发病率中约占 15%,具有传播快、增长迅速、恶性程度高的特点,主要表现为痰血、咳嗽、发热、胸痛、声音嘶哑等,目前发病机制和病因尚不明确,可能是由于致癌物损伤肺上皮细胞所导致[10-11]。虽然肺癌的治疗药物和方法发展得很快,但肺癌患者的 5 年生存率仍较低,其死亡率在我国恶性肿瘤中仍居第一位[12-13]。

化疗是一种全身性治疗的方式,而放疗是一种局部治疗的方式。有研究表明,化疗联合放疗可共同发挥作用,从而达到提高疗效的目的[14]。局限期 SCLC 主要采用放化疗治疗,理论上,增加放疗剂量,更有利于杀伤肿瘤细胞,有研究表明,放疗剂量的加大会增强肿瘤的灭杀,提高治疗效果[15]。还有研究发现放疗剂量增加,其毒副作用及对应的风险也随之增加[16]。本研究中,两组患者在常规化疗的基础上,均行超分割放疗,区别是观察组的放疗剂量适当进行了增加,研究结果表明,观察组患者总有效率显著优于对照组,两组患者虽然都有毒副反应,但多数为Ⅰ~Ⅱ级,不影响疗程,且两组的毒副反应的总发生率差异较小,提示适当增加放射剂量,可提高临床疗效,且并不增加毒副反应的风险,安全性较好。

本研究均为局限期 SCLC 患者,此时肿瘤未发生

转移和扩散,超分割放疗的疗效较好。由于肺癌细胞的生殖速度快,有研究表明,患者每推迟 1 d 接受治疗,其生存率就会降低约 2%[17]。超分割治疗可以降低总治疗的时间,从而降低肺癌细胞增殖的风险,提高患者生存率[18]。本研究结果显示,与对照组相比,观察组患者 1、2、3 年的局部控制率和生存率均显著升高;两组患者生活质量评分在治疗后均显著升高,且观察组高于对照组,提示适当加大剂量可以有效抑制肺癌细胞的增殖,提高疗效、患者的生存率和生活质量。有研究发现,适当增加放疗剂量可增强局部晚期非小细胞癌疗效,且不会增加毒副作用,安全性较高[19-20]。本研究结果与其相似。

综上所述,超分割放疗治疗局限期 SCLC 患者,适当加大分割剂量,则近远期疗效更好,局部控制率和生存率更好,且毒副反应未明显增高,安全性较好,可以提高患者的生活质量。但本研究也存在一定的局限性,选取的样本量较少,可能导致研究结果出现一定偏倚,后续应扩大样本量,进一步验证。

利益冲突　无

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本刊参考文献著录格式基本执行 GB/T 7714—2015《信息与文献 参考文献著录规则》。采用顺序编码制著录,依照其在文中出现的先后顺序用阿拉伯数字标出,并将序号置于方括号中,排列于文后。尽量避免引用摘要作为参考文献。引用文献(包括文字和表达的原意)务必请作者与原文核对无误。日文汉字请按日文规定书写,勿与我国汉字及简化字混淆。同一文献作者不超过 3 人者,全部著录用;超过 3 人,可以只著录前 3 人,后依文种加表示“,等”的文字。作者姓名一律姓氏在前,名字在后,国外作者的名字采用首字母缩写形式,缩写名后不加缩写点;不同作者姓名之间用“,”隔开,不用“和”、“and”等连词。外文期刊名称用缩写,以 *Index Medicus* 中的格式为准;中文期刊用全名。每条参考文献均须著录起止页。每年连续编码的期刊可以不著录期号。中文参考文献需同时有英文对照。

示例如下:

[1] 宋研,王国品.“保胆”还是“切胆”:对胆囊结石治疗的再思考[J].中国临床研究,2023,36(1):1-6.
Song Y, Wang GP. “Preserving gallbladder” or “cutting gallbladder”: Rethinking the treatment of gallstones[J]. Chin J Clin Res, 2023, 36(1): 1-6.

[2] Kim BJ, Hanna MH. Colorectal cancer in young adults[J]. J Surg Oncol, 2023, 127(8): 1247-1251.

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