·临床研究·

老年肺癌患者化疗期间睡眠障碍与免疫功能的相关性及非药物干预效果研究

汤玲,高苗*,左秀萍
(空军军医大学第一附属医院西京医院呼吸与危重症医学科,西安 771032)

【摘 要】 **目的** 分析老年肺癌患者化疗期间睡眠障碍与免疫功能的相关性,并评估非药物干预对睡眠障碍的应用效果。**方法** 对2022年1月至2024年12月空军军医大学第一附属医院西京医院收治的158例化疗的老年肺癌患者进行问卷调查,问卷内容包括睡眠质量[匹兹堡睡眠质量指数(PSQI)]、体能状态[Karnofsky体能状态评分(KPS)]、疲乏(癌症疲乏量表)、焦虑[广泛性焦虑量表(GAD-7)]、抑郁[9条目患者健康问卷(PHQ-9)]、疼痛[疼痛视觉模拟评分法(VAS)]。158例患者的有效回收率为95.57%(151/158),根据PSQI得分将老年肺癌患者分为睡眠障碍组(PSQI≥7分)与睡眠良好组(PSQI<7分)。比较两组患者基线资料及化疗前后免疫功能(T淋巴细胞亚群$CD4^+$、$CD8^+$、$CD4^+/CD8^+$),采用Pearson相关性分析老年肺癌化疗患者PSQI评分与各项指标的相关性;将睡眠障碍组采用随机数字表法分为观察组与对照组,对照组给予常规睡眠健康教育,观察组联合心理及运动干预,比较两组干预前及干预2周后睡眠质量(PSQI)和免疫功能($CD4^+$、$CD8^+$、$CD4^+/CD8^+$)变化。采用SPSS 26.0软件进行数据分析。根据数据类型,组间比较分别采用t检验、χ^2检验及Mann whitney U检验。**结果** 老年肺癌化疗患者睡眠障碍发生率为35.76%(54/151)。睡眠障碍组疲乏及GAD-7、PHQ-9、VAS评分均高于睡眠良好组($P<0.05$),化疗后$CD4^+$及$CD8^+$、$CD4^+/CD8^+$均低于睡眠良好组($P<0.05$)。Pearson相关性分析结果显示,老年肺癌化疗患者PSQI评分与疲乏评分、GAD-7评分、PHQ-9评分、VAS评分均呈显著正相关($r=0.543$、0.621、0.595、0.617;$P<0.05$),与化疗后$CD4^+$、化疗后$CD8^+$、化疗后$CD4^+/CD8^+$均呈显著负相关($r=-0.584$、-0.489、-0.427;$P<0.05$)。54例睡眠障碍组患者被随机分为观察组($n=27$例)与对照组($n=27$例),分别剔除1例、2例脱组病例。干预2周后,两组PSQI评分均较干预前降低($P<0.05$),且观察组干预后PSQI评分低于对照组($P<0.05$);两组干预前后$CD4^+$、$CD8^+$、$CD4^+/CD8^+$比较,差异均有统计学意义(均$P>0.05$)。**结论** 老年肺癌患者化疗期间睡眠障碍与免疫功能、疼痛、疲乏、焦虑、抑郁均有关,非药物睡眠干预对改善患者睡眠质量有利,但短期干预对免疫功能影响较小。

【关键词】 老年人;肺癌;化疗;睡眠质量;免疫功能
【中图分类号】 R563.9 【文献标志码】 A 【DOI】 10.11915/j.issn.1671-5403.2026.05.068

Correlation between sleep disorders and immune function in elderly patients with lung cancer during chemotherapy and effect of non-pharmacological intervention

Tang Ling, Gao Miao*, Zuo Xiuping
(Department of Respiratory and Critical Care Medicine, Xijing Hospital, the First Affiliated Hospital of Air Force Medical University, Xi′an 771032, China)

【**Abstract**】 **Objective** To analyze the correlation between sleep disorders and immune function in elderly patients with lung cancer during chemotherapy and to evaluate the application effect of non-pharmacological intervention on sleep disorders. **Methods** A questionnaire survey was conducted among 158 elderly lung cancer patients who received chemotherapy in Xijing Hospital, the First Affiliated Hospital of Air Force Military Medical University from January 2022 to December 2024. The questionnaire included sleep quality [Pittsburgh sleep quality index (PSQI)], physical status [Karnofsky performance status (KPS)], fatigue (cancer fatigue scale), anxiety [generalized anxiety disorder-7 (GAD-7)], depression [patient health questionnaire-9 (PHQ-9)], and pain [visual analogue scale (VAS)]. The effective recovery rate was 95.57% (151/158). According to PSQI score, the patients were divided into a sleep disorder group (PSQI≥7 points) and a good sleep group (PSQI<7 points). The baseline data and immune function (T lymphocyte subsets $CD4^+$, $CD8^+$, $CD4^+/CD8^+$) before and after chemotherapy were compared between the two groups. Pearson correlation analysis was used to assess the correlation between PSQI scores and each indicator in elderly lung cancer patients undergoing chemotherapy. The sleep disorder

收稿日期: 2025-05-24; **接受日期**: 2025-08-05
基金项目: 国家自然科学基金(82270526);陕西省级科技计划(2022SF-274)
通信作者: 高苗, E-mail: gaomiao0863@163.com

group was divided into an observation group and a control group using random number table method. The control group received routine sleep health education, while the observation group was received additional psychological and exercise interventions. Changes in sleep quality (PSQI) and immune function ($CD4^+$, $CD8^+$, $CD4^+/CD8^+$) before intervention and after 2 weeks of intervention were compared. SPSS 26.0 was used for statistical analysis. Data comparison between two groups was performed using t test, χ^2 test or Mann whitney U test depending on data type. **Results** The incidence rate of sleep disorders in elderly lung cancer patients undergoing chemotherapy was 35.76% (54/151). The scores of fatigue, GAD-7, PHQ-9, and VAS in the sleep disorder group were higher than those in the good sleep group ($P<0.05$), while $CD4^+$, $CD8^+$, and $CD4^+/CD8^+$ after chemotherapy were lower than those in the good sleep group ($P<0.05$). Pearson correlation analysis showed that PSQI scores in the elderly lung cancer patients undergoing chemotherapy was positively correlated with fatigue, GAD-7, PHQ-9, and VAS scores ($r=0.543$, 0.621, 0.595, 0.617; $P<0.05$), and negatively correlated with post-chemotherapy $CD4^+$, $CD8^+$, and $CD4^+/CD8^+$ ($r=-0.584$, -0.489, -0.427; $P<0.05$). The 54 patients in the sleep disorders were randomized into an observation group ($n=27$) and a control group ($n=27$), with 1 and 2 dropouts being excluded from the respective group. After 2 weeks of intervention, PSQI scores in both groups decreased compared with that before intervention ($P<0.05$), and PSQI scores in observation group after intervention were lower than that in the control group ($P<0.05$). There were no statistical differences in $CD4^+$, $CD8^+$, and $CD4^+/CD8^+$ between the two groups before and after intervention (all $P>0.05$). **Conclusion** Sleep disorders in elderly lung cancer patients during chemotherapy are related to immune function, pain, fatigue, anxiety, and depression. Non-pharmacological sleep interventions are beneficial for improving patients' sleep quality, but short-term intervention has little effect on immune function.

【Key words】 aged; lung cancer; chemotherapy; sleep quality; immune function

This work was supported by National Natural Science Foundation of China (82270526) *and Shaanxi Provincial Science and Technology Program* (2022SF-274).

Corresponding author: *Gao Miao*, *E-mail*: *gaomiao0863@163.com*

肺癌是全世界范围内发病率及致死率位居前列的恶性肿瘤,由于早期缺乏典型临床症状,中晚期肺癌在临床较为常见,化疗是中晚期肺癌的主要治疗手段,在延长患者生存期方面具有一定优势[1]。老年人是肺癌好发人群,随着全球老龄化进展的加快,老年肺癌患病人数也显著增多,老年患者器官功能退化,合并症多,疾病负担重,针对老年肺癌患者的临床调查是近年研究的热点[2]。化疗虽然有利于改善肺癌患者生存期,但可引起疼痛,并增加患者心理负担,可能影响中枢神经兴奋性,导致睡眠障碍[3]。近年有报道指出,出现睡眠障碍的肺癌化疗患者可能通过神经-内分泌-免疫轴途径影响机体免疫功能,积极改善患者睡眠质量对调节患者免疫功能有积极作用,但长期药物治疗可引起记忆力减退等不良反应,老年患者应谨慎使用药物干预睡眠障碍[4]。基于此,本研究分析老年肺癌化疗患者睡眠障碍与免疫功能的相关性,并评估非药物干预对睡眠障碍的应用效果。

1 对象与方法

1.1 研究对象

对2022年1月至2024年12月空军军医大学第一附属医院西京医院收治的158例化疗的老年肺癌患者进行问卷调查。纳入标准:(1)肺癌诊疗参考《中华医学会肿瘤学分会肺癌临床诊疗指南(2021版)》[5],为原发性Ⅲ~Ⅳ期肺癌,且接受化疗;(2)年龄≥60岁;(3)预计生存期≥6个月;(4)受教育程度为小学及以上,可配合问卷调查;(5)肺癌确诊至入组时间≥6个月;(6)自愿入组且均签署知情同意书。排除标准:(1)行肺癌根治术治疗;(2)合并其他恶性肿瘤;(3)合并精神分裂症等精神疾病;(4)合并免疫系统疾病;(5)合并肝功能衰竭等重要器官功能障碍;(6)合并恶液质、脑转移;(7)化疗前存在睡眠障碍。158例行化疗的老年肺癌患者共发放158份问卷,有7份因选项有规律性或全部填写为同一选项判断为无效问卷,予以剔除,有效回收率为95.57%(151/158)。本研究获得空军军医大学第一附属医院西京医院医学伦理委员会审批(伦理批号:202111-XH-003)。研究符合《赫尔辛基宣言》。

1.2 方法

1.2.1 问卷调查方法 在老年肺癌患者当前化疗周期结束时,于安静整洁且无其他人的病房内接受问卷调查,由研究者面对面、一对一进行。(1)匹兹堡睡眠质量指数[6]:匹兹堡睡眠质量指数(Pittsburgh sleep quality index, PSQI)共有18个计分条目,总得分范围为0~21分,得分越高,睡眠障碍越严重,PSQI≥7分被认为存在睡眠障碍,并以此将老年肺癌患者分为睡眠障碍组(PSQI≥7分)与睡眠良好组(PSQI<7分)。(2)Karnofsky体能状态评分[7]:Karnofsky体能状态评分(Karnofsky performance status, KPS)量表总得分范围为0~100分,得分越高,体能状态越好。(3)癌症疲乏量表[8]:癌症疲乏量表量表包含15个条目,总得分范围为0~60分,得分越高,癌因性疲乏越严重。(4)广泛性焦虑量表[9]:广

泛性焦虑量表(generalized anxiety disorder-7, GAD-7)包含 7 个条目,满分 21 分,得分越高,焦虑表现越严重。(5)9 条目患者健康问卷[10]:9 条目患者健康问卷(patient health questionnaire-9, PHQ-9)量表包含 9 个条目,满分 27 分,得分越高,抑郁表现越严重。(6)疼痛视觉模拟评分[11]:疼痛视觉模拟评分(visual analogue scale,VAS)量表评分范围 0~10 分,得分越高,疼痛越严重。

1.2.2 实验室指标检查方法 在化疗前及问卷调查当日(化疗后),采集空腹外周肘静脉血,使用流式细胞仪(美国 BD 公司,型号:FACS Canto)检测 T 淋巴细胞亚群 $CD4^+$、$CD8^+$水平,并计算 $CD4^+/CD8^+$。

1.2.3 化疗疗效评价 参考《中华医学会肿瘤学分会肺癌临床诊疗指南(2021 版)》[5],以实体瘤疗效标准评估化疗疗效,以治疗前后胸部 CT 图像变化评估,分为完全缓解(病灶消失且维持 4 周以上)、部分缓解(病灶直径减少>30%)、疾病稳定(介于部分缓解与疾病进展之间)及疾病进展(病灶直径>20%或出现新病灶)。

1.2.4 睡眠障碍干预方法 由 2 名非研究者完成随机分组匹配,分配前保密分配序列,将睡眠障碍组的老年肺癌患者采用随机数字表余数分组法分为观察组($n=27$)与对照组($n=27$)。参考《癌症生存者睡眠障碍指南》[12],对照组给予常规睡眠健康教育,包括保持规律的作息时间、健康饮食和规律的日间锻炼,保证睡眠环境安静,睡前避免小睡、兴奋性饮食、过多的液体或刺激性活动,并改变对睡眠无益的信念。观察组在上述基础上联合心理及运动干预:联合家属及心理咨询师增加对老年肺癌患者的情感支持,缓解患者对肺癌及化疗的担忧及焦虑情绪,提升治疗信心;指导老年患者进行身心放松训练,包括渐进式肌肉放松、腹式呼吸等,每次 15~30 min,3 次/d;指导老年患者行哈达瑜伽运动,60~90 min/次,5 次/周。质量控制:两组患者均由同一组研究者完成上述干预,在干预前参考《癌症生存者睡眠障碍指南》对睡眠干预相关知识进行培训,干预期间记录患者的不依从行为,对坚持兴奋性饮食、拒绝身心放松训练等不配合者予以剔除。在干预前(即问卷调查当日)及干预 2 周后,检测睡眠质量(PSQI)、免疫功能,评估干预效果。

1.3 统计学处理

采用 SPSS 26.0 统计软件进行数据分析。符合正态分布的计量资料以均数±标准差($\bar{x}\pm s$)表示,组间比较采用 t 检验。计数资料以例数(百分率)表示,组间比较采用 χ^2 检验,治疗效果为等级资料,采用 Mann whitney U 检验。采用 Pearson 相关性分析评估老年肺癌化疗患者 PSQI 评分与各项指标的相关性。$P<0.05$ 为差异有统计学意义。

2 结 果

2.1 睡眠障碍组与睡眠良好组患者的一般资料

151 例老年肺癌化疗患者睡眠障碍发生率为 35.76%(54/151)。睡眠障碍组患者疲乏、GAD-7、PHQ-9 及 VAS 评分均高于睡眠良好组($P<0.05$),化疗后 $CD4^+$、$CD8^+$及 $CD4^+/CD8^+$均低于睡眠良好组($P<0.05$);其余指标比较,差异均无统计学意义($P>0.05$;表 1)。

2.2 老年肺癌化疗患者 PSQI 评分与各项指标的相关性

Pearson 相关性分析结果显示,老年肺癌化疗患者 PSQI 评分与疲乏评分、GAD-7 评分、PHQ-9 评分、VAS 评分均呈显著正相关($P<0.05$);与化疗后 $CD4^+$、$CD8^+$、$CD4^+/CD8^+$均呈显著负相关($P<0.05$;表 2)。

2.3 观察组与对照组患者干预前后睡眠质量及免疫功能

观察组与对照组基线资料比较,差异均无统计学意义(均 $P>0.05$,表 3),均衡可比。观察组与对照组患者在 2 周的干预期间因不配合干预、拒绝再次接受问卷调查等分别出现 1 例、2 例脱组病例,予以剔除。干预 2 周后,两组患者 PSQI 评分均较干预前降低($P<0.05$),且观察组患者干预后 PSQI 评分低于对照组($P<0.05$);两组患者干预前后 $CD4^+$、$CD8^+$、$CD4^+/CD8^+$比较,差异均无统计学意义($P>0.05$;表 4)。

3 讨 论

研究发现,恶性肿瘤患者睡眠障碍发生率较一般人群更高,由癌症及治疗引起的疼痛、疾病本身、情绪因素等是影响睡眠障碍的重要因素[13]。老年肺癌患者在化疗期间,常出现心理压力及疲乏感增加,疼痛加剧,导致昼夜生理节律紊乱,睡眠质量较差,有报道指出,肺癌患者在抗肿瘤治疗期间的睡眠障碍发生率可超过 50%[14]。不仅如此,睡眠障碍已是公认的肺癌生存预测因素,睡眠障碍还能影响神经内分泌系统,通过介导糖皮质激素灵敏性及皮质醇压力反应,增强炎症反应,影响抗肿瘤疗效及安全性,对肺癌患者预后有不利影响[15]。杨淑君等[16]研究发现,睡眠时间<7 h 是肺癌患者化疗相关恶心呕吐发生的危险因素,明确指出睡眠质量可影响肺

表1 睡眠障碍组与睡眠良好组患者一般资料比较

Table 1 Comparison of general data between sleep disorder group and good sleep group

Item	Sleep disorder group (n=54)	Good sleep group (n=97)	t/χ^2	P value
Gender[n(%)]			0.004	0.953
Male	32(59.26)	57(58.76)		
Female	22(40.74)	40(41.24)		
Age(years, $\bar{x}\pm s$)	71.26±5.36	69.86±4.89	1.629	0.106
Education level[n(%)]			1.811	0.404
Primary school	12(22.22)	19(19.59)		
Junior and senior high schools	36(66.67)	59(60.82)		
Junior college or above	6(11.11)	19(19.59)		
Payment method of medical expense[n(%)]			0.505	0.777
Urban medical insurance/new rural cooperative medical care system	39(72.22)	69(71.13)		
Commercial insurance	8(14.81)	18(18.56)		
Self-paying	7(12.96)	10(10.31)		
Smoking history[n(%)]	18(33.33)	31(31.96)	0.030	0.863
Alcohol drinking history[n(%)]	14(25.93)	21(21.65)	0.356	0.551
Hypertension[n(%)]	17(31.48)	28(28.87)	0.113	0.736
Diabetes mellitus[n(%)]	6(11.11)	9(9.28)	0.130	0.718
Coronary heart disease[n(%)]	8(14.81)	11(11.34)	0.381	0.537
Pathological type[n(%)]			1.168	0.558
Adenocarcinoma	18(33.33)	37(38.14)		
Squamous carcinoma	28(51.85)	51(52.58)		
Small cell carcinoma	8(14.81)	9(9.28)		
TNM staging[n(%)]			0.272	0.602
Ⅲ	26(48.15)	51(52.58)		
Ⅳ	28(51.85)	46(57.42)		
Chemotherapy regimen[n(%)]			0.045	0.978
Pemetrexed+carboplatin	24(44.44)	42(43.30)		
Paclitaxel+carboplatin	18(33.33)	32(32.99)		
Vinorelbine+cisplatin	12(22.22)	23(23.71)		
Number of chemotherapy cycle[n(%)]			0.631	0.729
4	27(50.00)	55(56.70)		
5	22(40.74)	34(35.05)		
6	5(9.26)	8(8.25)		
Therapeutic effect[n(%)]			0.088	0.930
Complete remission	0(0.00)	0(0.00)		
Partial remission	17(31.48)	29(29.90)		
Stable disease	27(50.00)	53(54.64)		
Progressive disease[n(%)]	10(18.52)	15(15.46)		
KPS score(points, $\bar{x}\pm s$)	72.49±7.16	74.16±6.57	1.449	0.149
Fatigue score(points, $\bar{x}\pm s$)	24.98±4.05	19.73±3.48	8.373	<0.001
GAD-7 score(points, $\bar{x}\pm s$)	8.79±1.45	6.08±1.24	12.105	<0.001
PHQ-9 score(points, $\bar{x}\pm s$)	9.35±1.87	7.24±1.35	7.992	<0.001
VAS score(points, $\bar{x}\pm s$)	2.89±0.55	2.31±0.51	6.512	<0.001
$CD4^+$ before chemotherapy(%, $\bar{x}\pm s$)	44.49±6.98	45.08±6.44	0.524	0.601
$CD8^+$ before chemotherapy(%, $\bar{x}\pm s$)	34.21±3.82	34.93±3.57	1.158	0.249
$CD4^+/CD8^+$ before chemotherapy(x±s)	1.31±0.24	1.30±0.20	0.274	0.785
$CD4^+$ after chemotherapy(%, $\bar{x}\pm s$)	31.15±5.79	39.42±6.18	8.059	<0.001
$CD8^+$ after chemotherapy(%, $\bar{x}\pm s$)	27.45±5.17	32.69±6.05	5.365	<0.001
$CD4^+/CD8^+$ after chemotherapy(x±s)	1.15±0.21	1.24±0.23	2.376	0.019

TNM: tumor node metastasis; KPS: Karnofsky performance status; GAD-7: generalized anxiety disorder-7; PHQ-9: patient health questionnaire-9; VAS: visual analogue scale.

表 2 PSQI 评分与各项指标的相关性分析

Table 2 Correlation between PSQI score and various indicators

Item	r	P value
Fatigue score	0.543	<0.001
GAD-7 score	0.621	<0.001
PHQ-9 score	0.595	<0.001
VAS score	0.617	<0.001
$CD4^+$ after chemotherapy	−0.584	<0.001
$CD8^+$after chemotherapy	−0.489	<0.001
$CD4^+/CD8^+$ after chemotherapy	−0.427	<0.001

PSQI: Pittsburgh sleep quality index; GAD-7: generalized anxiety disorder-7; PHQ-9: patient health questionnaire-9; VAS: visual analogue scale.

表 3 观察组与对照组基线资料比较

Table 3 Comparison of baseline data between observation group and control group ($n=27$)

Item	Observation group	Control group	t/χ^2	P value
Gender[n(%)]			0.307	0.580
Male	17(62.96)	15(55.56)		
Female	10(37.04)	12(44.44)		
Age(years, $\bar{x}\pm s$)	71.39±5.40	71.13±5.27	0.179	0.859
Pathological type[n(%)]			0.365	0.833
Adenocarcinoma	8(29.63)	10(37.04)		
Squamous carcinoma	15(55.56)	13(48.15)		
Small cell carcinoma	4(14.81)	4(14.81)		
TNM staging[n(%)]			0.297	0.586
Ⅲ	12(44.44)	14(51.85)		
Ⅳ	15(55.56)	13(48.15)		
Chemotherapy regimen[n(%)]			0.389	0.823
Pemetrexed+carboplatin	11(40.74)	13(48.15)		
Paclitaxel+carboplatin	10(37.04)	8(29.63)		
Vinorelbine+cisplatin	6(22.22)	6(22.22)		
Number of chemotherapy cycle [n(%)]			0.419	0.811
4	14(51.85)	13(48.15)		
5	10(37.04)	12(44.44)		
6	3(11.11)	2(7.41)		
Therapeutic effect[n(%)]			0.096	0.953
Partial remission	8(29.63)	9(33.33)		
Stable disease	14(51.85)	13(48.15)		
Progressive disease	5(18.52)	5(18.52)		
PSQI score(points, $\bar{x}\pm s$)	11.36±2.02	11.19±1.87	0.321	0.750
KPS score(points, $\bar{x}\pm s$)	72.86±7.05	72.12±7.39	0.376	0.708
Fatigue score(points, $\bar{x}\pm s$)	25.19±3.98	24.76±4.11	0.391	0.698
GAD-7 score(points, $\bar{x}\pm s$)	8.86±1.40	8.71±1.49	0.381	0.705
PHQ-9 score(points, $\bar{x}\pm s$)	9.48±1.98	9.22±1.76	0.510	0.612
VAS score(points, $\bar{x}\pm s$)	2.95±0.52	2.82±0.57	0.876	0.385

PSQI: Pittsburgh sleep quality index; KPS: Karnofsky performance status; GAD-7: generalized anxiety disorder-7; PHQ-9: patient health questionnaire-9; VAS: visual analogue scale.

表 4 观察组与对照组患者干预前后 PSQI 评分及 $CD4^+$、$CD8^+$、$CD4^+/CD8^+$指标比较

Table 4 Comparison of PSQI score and $CD4^+$, $CD8^+$and $CD4^+/CD8^+$before and after intervention in observation group and control group ($\bar{x}\pm s$)

Group	n	PSQI score(points)		$CD4^+$(%)	
		Before intervention	After 2 weeks of intervention	Before intervention	After 2 weeks of intervention
Observation	26	12.46±2.19	9.06±1.24*	31.10±5.56	32.09±5.49
Control	25	12.31±2.23	11.19±1.65*	31.18±5.80	31.69±5.18
t		0.242	5.225	0.050	0.267
P value		0.810	<0.001	0.960	0.790

Group	n	$CD8^+$(%)		$CD4^+/CD8^+$	
		Before intervention	After 2 weeks of intervention	Before intervention	After 2 weeks of intervention
Observation	26	27.61±5.24	27.98±5.06	1.15±0.20	1.19±0.22
Control	25	27.41±5.13	27.66±4.87	1.16±0.21	1.17±0.21
t		0.138	0.230	0.174	0.332
P value		0.891	0.819	0.862	0.741

PSQI: Pittsburgh sleep quality index. Compared with before intervention, * $P<0.05$.

癌化疗相关症状。本研究也就老年肺癌患者化疗期间睡眠障碍发生情况展开分析,发现其睡眠障碍发生率为 35.76%,虽然睡眠障碍组与睡眠良好组化疗方案及疗效并无显著差异,但睡眠障碍组化疗后 $CD4^+$、$CD8^+$及 $CD4^+/CD8^+$均低于睡眠良好组,提示老年肺癌化疗患者睡眠障碍值得临床关注,可能与老年肺癌患者细胞免疫应答受到抑制密切相关。目前,肺癌患者睡眠障碍的报道较为多见,但睡眠障碍与肺癌患者免疫功能的相关性研究较为少见。分析老年肺癌患者细胞免疫应答与睡眠障碍的相关性原因可能为睡眠障碍通过影响促肾上腺素活性,调节免疫细胞的增殖及分化,导致细胞免疫抑制,细胞免疫抑制又能通过影响机体炎症反应调控神经内分泌系统,参与睡眠障碍的发生[17]。

另外,本研究还发现,老年肺癌化疗患者 PSQI 评分与化疗后 $CD4^+$、$CD8^+$及 $CD4^+/CD8^+$均呈显著负相关,提示老年肺癌患者化疗期间睡眠障碍与细胞免疫功能抑制可能密切相关。分析其原因可能为细胞免疫功能受限引起炎症因子释放增多,影响 5-羟色胺等神经递质的分泌,诱导睡眠紊乱,而睡眠障碍又通过介导神经内分泌系统,影响细胞免疫应答,形成恶性循环[18]。另据文献报道,疼痛可作为应激源,作用于神经内分泌系统,刺激交感神经兴奋性升高,影响昼夜生理节律,导致睡眠质量下降,而睡眠障碍又易引起神经衰弱,导致患者对疼痛耐受性下降,主观疼痛感升高,故疼痛与睡眠障碍可能具有双向关系[19]。本研究中,老年肺癌化疗患者 PSQI 评分与 VAS 评分呈显著正相关,提示老年肺癌化疗患者睡眠障碍与疼痛可能具有相互促进作用,与国内报道结果相似[20]。本研究还发现,老年肺癌化疗患者 PSQI 评分与

GAD-7及PHQ-9评分均呈显著正相关,提示患者睡眠障碍还与焦虑、抑郁情绪具有较强的关相性。该结果原因可能为焦虑及抑郁引起自主神经功能紊乱,导致下丘脑-垂体-肾上腺轴功能亢进,夜间唤醒系统过度兴奋,导致入睡困难及夜间觉醒次数增加,影响睡眠质量,睡眠障碍则通过影响神经内分泌系统,介导5-羟色胺的释放,增加负性情绪的产生,故二者呈正相关[21]。此外,老年肺癌化疗患者PSQI评分与疲乏评分也呈显著正相关,其原因可能为疲乏易引起白天嗜睡,干扰患者正常的睡眠周期,而睡眠障碍导致患者难以充分休息,进一步增加疲乏,形成双向的不良影响[22]。因此,老年肺癌化疗患者在对睡眠质量进行干预时,应同时考虑疼痛、疲乏、焦虑、抑郁与睡眠障碍的相关性,针对性予以疼痛管理、疲乏及心理干预,可能对促进睡眠质量改善有积极作用。

根据上述结果可考虑为睡眠障碍者提供心理、身心放松训练等干预措施,以综合缓解与睡眠障碍有关的不良因素,以尽快改善患者睡眠质量,本研究也在常规睡眠健康教育的基础上联合心理及放松训练等干预措施,以提高睡眠干预效果。此外,由于肺癌患者免疫功能相关因素较多,长期睡眠干预观察期间患者治疗效果、疼痛等均可能随时间的延长而出现较大变化,为避免多种混杂因素的影响,本研究仅观察2周的干预效果。结果显示,观察组干预后PSQI评分低于对照组,提示非药物治疗对减轻患者睡眠障碍有积极作用,对于老年肺癌患者,在化疗期间可积极给予教育、心理、运动干预等针对性非药物睡眠管理,以改善睡眠质量,减少睡眠障碍对患者身心的不良影响。两组干预前及干预2周后$CD4^+$、$CD8^+$、$CD4^+/CD8^+$未出现明显变化,考虑与干预时间较短,对免疫功能的影响较小有关。故非药物干预对老年肺癌化疗患者免疫功能的影响还需后续延长干预时间的进一步探究,同时也需要对等疼痛、体能状态等混杂因素严格控制,以提高结果的严谨性。此外,本研究作为单中心小样本量研究,研究结果可能存在偏倚,在可靠性、代表性方面存在一定欠缺,未来还需大样本量多中心研究对本研究结果加以验证。

综上,老年肺癌患者化疗期间睡眠障碍值得临床关注,不仅与免疫功能呈双向关系,还与疼痛、疲乏、焦虑、抑郁均有关。非药物睡眠管理对减轻患者睡眠障碍有利,可为临床管理提供参考信息。

【参考文献】

[1] Zhou T, Wang Z, Qiao C, *et al*. Sleep disturbances and the risk of lung cancer: a meta-epidemiological study[J]. BMC Cancer, 2023, 23(1): 884-894. DOI: 10.1186/s12885-023-11392-2.

[2] Temel JS, Jackson VA, El-Jawahri A, *et al*. Stepped palliative care for patients with advanced lung cancer: a randomized clinical trial[J]. JAMA, 2024, 332(6): 471-481. DOI: 10.1001/jama.2024.10398.

[3] Takemura N, Cheung DST, Fong DYT, *et al*. Effectiveness of aerobic exercise and tai chi interventions on sleep quality in patients with advanced lung cancer: a randomized clinical trial[J]. JAMA Oncol, 2024, 10(2): 176-184. DOI: 10.1001/jamaoncol.2023.5248.

[4] Shi J, Wen W, Long J, *et al*. Genetic correlation and causal associations between psychiatric disorders and lung cancer risk[J]. J Affect Disord, 2024, 356(1): 647-656. DOI: 10.1016/j.jad.2024.04.080.

[5] 中华医学会肿瘤学分会, 中华医学会杂志社. 中华医学会肿瘤学分会肺癌临床诊疗指南(2021版)[J]. 中华医学杂志, 2021, 101(23): 1725-1757. DOI: 10.3760/cma.j.cn112137-20210207-00377.

[6] Setyowati A, Chung MH. Validity and reliability of the indonesian version of the Pittsburgh sleep quality index in adolescents[J]. Int J Nurs Pract, 2021, 27(5): e12856. DOI: 10.1111/ijn.12856.

[7] Shamseddeen H, Pike F, Ghabril M, *et al*. Karnofsky performance status predicts outcomes in candidates for simultaneous liver-kidney transplant[J]. Clin Transplant, 2021, 35(2): e14190. DOI: 10.1111/ctr.14190.

[8] 张凤玲, 丁玥, 韩丽沙. 癌症疲乏量表中文版的信效度[J]. 中国心理卫生杂志, 2011, 25(11): 810-813. DOI: 10.3969/j.issn.1000-6729.2011.11.003.

[9] Zinchuk M, Kustov G, Pashnin E, *et al*. Validation of the generalized anxiety disorder-7 (GAD-7) in Russian people with epilepsy[J]. Epilepsy Behav, 2021, 123(1): e108269. DOI: 10.1016/j.yebeh.2021.108269.

[10] Costantini L, Pasquarella C, Odone A, *et al*. Screening for depression in primary care with patient health questionnaire-9 (PHQ-9): a systematic review[J]. J Affect Disord, 2021, 279(1): 473-483. DOI: 10.1016/j.jad.2020.09.131.

[11] Huang Q, Lin J, Han R, *et al*. Using virtual reality exposure therapy in pain management: a systematic review and meta-analysis of randomized controlled trials[J]. Value Health, 2022, 25(2): 288-301. DOI: 10.1016/j.jval.2021.04.1285.

[12] Palesh O, Solomon N, Hofmeister E, *et al*. A novel approach to management of sleep-associated problems in patients with breast cancer (MOSAIC) during chemotherapy: a pilot study[J]. Sleep, 2020, 43(10): zsaa070. DOI: 10.1093/sleep/zsaa070.

[13] 吴绒, 侯丽华, 任亚如. 老年食管癌患者放疗期间生活质量的动态观察[J]. 中华老年多器官疾病杂志, 2025, 24(2): 93-98. DOI: 10.11915/j.issn.1671-5403.2025.02.019.

[14] Ruan GT, Wei YP, Ge YZ, *et al*. Poor sleep quality association with higher lung cancer risk: a nested case-control study[J]. PeerJ, 2023, 11(1): e16540. DOI: 10.7717/peerj.16540.

[15] Zhou Q, Pan Y, Yang X, *et al*. Neoadjuvant SHR-1701 with or without chemotherapy in unresectable stage Ⅲ non-small-cell lung cancer: a proof-of-concept, phase 2 trial[J]. Cancer Cell, 2024, 42(7): 1258-1267.e2. DOI: 10.1016/j.ccell.2024.05.024.

[16] 杨淑君, 巴佳代子, 薛琼, 等. 睡眠时长对肺癌患者化疗相关症状的影响分析[J]. 心肺血管病杂志, 2024, 43(9): 963-966, 971. DOI: 10.3969/j.issn.1007-5062.2024.09.10.

[17] Prieur-Drevon D, Pabst L, Mascaux C, *et al*. Sleep quality in lung cancer and specifically non-small-cell lung cancer: a rapid review[J]. Support Care Cancer, 2025, 33(2): 123-129. DOI: 10.1007/s00520-024-09139-1.

[18] Donzella SM, Deubler E, Patel AV, *et al*. Sleep and cancer mortality in the cancer prevention study-Ⅱ[J]. Cancer Causes Control, 2024, 35(12): 1541-1555. DOI: 10.1007/s10552-024-01910-3.

[19] Freund W, Weber F. The function of sleep and the treatment of primary insomnia[J]. Dtsch Arztebl Int, 2023, 120(50): 863-870. DOI: 10.3238/arztebl.m2023.0228.

[20] 胡菲, 阳华, 阳婷, 等. 基于决策树模型分析肺癌化疗患者睡眠障碍发生的危险因素及护理对策[J]. 中华全科医学, 2024, 22(12): 2158-2161. DOI: 10.16766/j.cnki.issn.1674-4152.003820.

[21] Zhou Z, Yang Y, Sun J, *et al*. Heterogeneity of pain-fatigue-sleep disturbance symptom clusters in lung cancer patients after chemotherapy: a latent profile analysis[J]. Support Care Cancer, 2024, 32(12): 821-829. DOI: 10.1007/s00520-024-09032-x.

[22] Williamson TJ, Garon EB, Irwin MR, *et al*. Sleep disturbance as a mediator of lung cancer stigma on psychological distress and physical symptom burden[J]. Psychosom Med, 2024, 86(4): 334-341. DOI: 10.1097/PSY.0000000000001299.

(编辑: 温玲玲)