

哮喘患者合并焦虑、抑郁症状的临床特征及心理干预疗效评价

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【摘要】 目的 分析哮喘患者合并焦虑、抑郁症状的患病情况及其与症状控制、过敏性合并症的关系,并评价心理干预对患者的心理健康及哮喘控制的作用。方法 纳入2020年12月至2024年7月在复旦大学附属中山医院就诊并进行心理评估的231例哮喘患者,通过问卷调查收集患者的一般资料、哮喘疾病信息、过敏性合并症、9项患者健康问卷抑郁量表(Patient Health Questionnaire-9, PHQ-9)和广泛性焦虑量表(General Anxiety Disorder-7, GAD-7)评分等。采用Wilcoxon秩和检验和卡方检验比较不同焦虑、抑郁症状哮喘患者的临床特征。利用多因素Logistic回归分析焦虑、抑郁症状与哮喘控制、急性发作、过敏性合并症的相关性。52例哮喘患者于门诊接受治疗团队提供的个性化心理干预,采用线性混合效应模型分析心理干预对哮喘控制和心理健康的作用。结果 231例哮喘患者中,16例(6.93%)仅合并抑郁症状,28例(12.12%)仅合并焦虑症状,72例(31.17%)同时合并焦虑和抑郁症状。相较于无焦虑、抑郁症状的患者,合并焦虑、抑郁症状的哮喘患者更年轻、未婚居多、有胸闷症状、急性发作频繁、有过敏性合并症(P 均 <0.05),两组之间哮喘病程、肺功能及呼出气一氧化氮(fractional exhaled nitric oxide, FeNO)的差异均无统计学意义。多因素Logistic回归分析表明,焦虑、抑郁症状与哮喘控制不佳(焦虑:OR=1.93, 95%CI: 1.03~3.63, $P=0.040$;抑郁:OR=3.77, 95%CI: 2.01~7.19, $P<0.001$)、哮喘急性发作(焦虑:OR=4.30, 95%CI: 1.78~10.38, $P<0.001$;抑郁:OR=1.22, 95%CI: 1.08~1.61, $P=0.003$)显著相关。哮喘患者的过敏性合并症与焦虑症状显著相关(OR=1.80, 95%CI: 1.15~2.82, $P=0.010$),而与抑郁症状未见显著关联。52例患者接受心理干预后,哮喘控制评分(Asthma Control Test, ACT)、哮喘生活质量调查问卷评分(mini Asthma Quality of Life Questionnaire, miniAQLQ)、PHQ-9和GAD-7评分均有显著改善(P 均 <0.001)。结论 焦虑、抑郁症状在哮喘患者中常见,并与哮喘急性发作、症状控制不佳和生活质量下降密切相关,合并过敏性疾病和哮喘患者发生焦虑症状显著相关,心理干预是改善哮喘控制和心理健康的可行途径。

【关键词】 哮喘; 焦虑; 抑郁; 过敏性合并症; 心理干预

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Clinical characteristics and efficacy evaluation of psychological interventions in asthmatic patients with anxiety and depression

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【Abstract】 **Objective** To analyze the depression and anxiety situation in asthmatic patients and their

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relationship with asthma symptom control and allergic comorbidities, and to evaluate the effects of psychological interventions on mental health and asthma control. **Methods** Between Dec 2020 and Jul 2024, 231 asthmatic patients were enrolled and underwent mental assessment in Zhongshan Hospital, Fudan University. Data on demographics, asthma characteristics, allergic comorbidities, Patient Health Questionnaire-9 (PHQ-9), and Generalized Anxiety Disorder-7 (GAD-7) scores were collected via questionnaires. The Wilcoxon rank-sum test and chi-square test were used to compare clinical characteristics of patients with different anxiety and depression statuses. Multivariate logistic regression was employed to analyze the associations of anxiety and depression with asthma control, acute exacerbations, and allergic comorbidities. Fifty-two patients received psychological interventions provided by psychiatrists, and improvements in asthma control and mental health were evaluated before and after treatment. A linear mixed-effects model was applied to evaluate the improvement after psychological interventions. **Results** Among 231 asthmatic patients, 16 cases (6.93%) had depression alone, 28 cases (12.12%) had anxiety alone, and 72 cases (31.17%) exhibited comorbid anxiety and depression. Patients with anxiety or depression were younger, more likely to be unmarried, reported chest tightness, experienced frequent acute exacerbations, and had more allergic comorbidities (all $P < 0.05$), though no significant differences were observed in asthma duration, lung function, or fractional exhaled nitric oxide (FeNO). Multivariate Logistic regression indicated that both anxiety and depression were significantly associated with poor asthma control (anxiety: OR=1.93, 95%CI: 1.03–3.63, $P=0.040$; depression: OR=3.77, 95%CI: 2.01–7.19, $P < 0.001$), and acute exacerbations (anxiety: OR=4.30, 95%CI: 1.78–10.38, $P < 0.001$; depression: OR=1.22, 95%CI: 1.08–1.61, $P=0.003$). Allergic comorbidities were significantly associated with anxiety (OR=1.80, 95%CI: 1.15–2.82, $P=0.010$) but not with depression. After psychological interventions, the 52 patients showed significant improvements in Asthma Control Test (ACT), mini Asthma Quality of Life Questionnaire (miniAQLQ), PHQ-9 and GAD-7 scores (all $P < 0.001$). **Conclusion** Anxiety and depression are prevalent in asthmatic patients and are strongly associated with acute exacerbations, suboptimal symptom control, and reduced quality of life. Allergic comorbidities are significantly linked to the increased risk of anxiety. Psychological interventions represent a feasible strategy to improve asthma control and mental well-being outcomes.

【Key words】 asthma; anxiety; depression; allergic comorbidity; psychological intervention

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哮喘是一种以慢性气道炎症及气道高反应性为主要特征的呼吸系统疾病,全球约有3亿哮喘患者^[1]。随着生物-心理-社会医学模式的发展,哮喘被定义为一种典型的心身疾病^[2]。反复发作的气喘、咳嗽、胸闷等症状严重影响哮喘患者的生活质量和社会活动,进而影响患者的心理健康。流行病学研究表明,心理疾病在哮喘患者中普遍存在,尤其是焦虑、抑郁,且哮喘是焦虑、抑郁的重要危险因素^[3-4]。合并焦虑或抑郁的哮喘患者常存在哮喘控制水平低下、急性发作频率增加等问题^[5]。因此,深入探究焦虑、抑郁对哮喘患者的全面管理和临床诊

疗具有重要意义。

尽管哮喘与过敏性合并症(如鼻炎、鼻窦炎、荨麻疹)的共病现象已引起广泛关注,但关于焦虑、抑郁与哮喘患者过敏性合并症的研究仍相对缺乏。心理干预能否改善合并焦虑或抑郁患者的哮喘控制目前尚无定论。基于此,本研究旨在探讨:(1)合并焦虑、抑郁症状的哮喘患者在社会人口学、哮喘疾病情况、过敏性合并症数量及种类上的特征差异;(2)心理干预对改善患者哮喘症状与心理健康的协同效应。以期为中国哮喘人群焦虑、抑郁症状的临床管理提供实践经验。

资料和方法

研究对象 本研究为真实世界观察性研究,纳入2020年12月至2024年7月在复旦大学附属中山医院就诊并接受心理健康状况评估的231例哮喘患者。入组标准:(1)符合《支气管哮喘防治指南(2020年版)》哮喘诊断标准^[6];(2)可独立完成问卷调查。排除标准:(1)合并其他肺部基础疾病(慢性阻塞性肺病,支气管扩张,肺肿瘤等);(2)合并严重的其他系统疾病。所有患者均知晓研究内容并签署知情同意书。本研究方案经复旦大学附属中山医院医学伦理委员会审批通过(批准号:B2019-020R)。

研究方法

收集资料 收集入组患者的基本社会人口学特征(年龄、性别、婚姻状况、教育程度、BMI)、哮喘疾病信息(病程、症状、基础用药、过去3个月内急性发作次数)、过敏性合并症(鼻炎、鼻窦炎、过敏性皮炎、荨麻疹、结膜炎)、入组后基线肺功能[第一秒用力呼气容积(forced expiratory volume in first second, FEV₁)、FEV₁占预计值百分比(percentage of predicted FEV₁, FEV₁%pred)、用力肺活量(forced vital capacity, FVC)、FEV₁/FVC]、支气管舒张试验(吸入支气管舒张剂后FEV₁%pred的改善情况)、呼出气一氧化氮(fractional exhaled nitric oxide, FeNO)等信息。根据2024年全球哮喘防治倡议(Global Initiative for Asthma, GINA),将患者的哮喘治疗等级分为1~2级、3级、4级、5级。记录患者的哮喘控制评分(Asthma Control Test, ACT)和哮喘生活质量调查问卷评分(mini Asthma Quality of Life Questionnaire, miniAQLQ)。哮喘控制评价:

ACT评分 ≥ 20 分认为控制良好,16~19分认为控制不佳,5~15分认为控制很差。采用广泛性焦虑量表(General Anxiety Disorder-7, GAD-7)和9项患者健康问卷抑郁量表(Patient Health Questionnaire-9, PHQ-9)分别评估患者的焦虑和抑郁症状。GAD-7总分 > 4 分认为有焦虑症状,PHQ-9总分 > 4 分认为有抑郁症状。

心理行为干预和心理药物治疗 这部分属于前瞻性观察性研究,基于过敏性疾病的复杂性和心理交互性,我院变态反应多学科门诊联合变态反应科、心理医学科、皮肤科、耳鼻咽喉科等为过敏性疾病患者提供多学科联合的精准诊疗。共52例患者就诊于变态反应多学科门诊并接受心理干预,心理医学科医师依据患者情况提供的个性化治疗,包括药物和非药物干预。药物治疗根据患者临床症状特点选择相应的抗焦虑及抗抑郁药(表1)。心理行为干预包括支持性心理干预、基于网络指导正念冥想(一次20 min,一天2~4次)、腹式呼吸训练(一天3次,90次/周期)、渐进肌肉放松训练(一次20 min,一天2~3次)等。疾病管理中增加行为激活,增加可自我掌控及愉悦的生活事件,如唱歌、运动等帮助患者改善情绪及呼吸功能。采用Morisky用药依从性量表(Morisky Medication Adherence Scale-4 item, MMAS-4)评估患者的用药依从性:0分为高依从性,1~2分为中等依从性,3~4分为低依从性。心理干预后1~3个月内对患者进行问卷调查及电话随访,分别采集心理干预前后的ACT、miniAQLQ、PHQ-9和GAD-7评分,同时收集患者对心理干预改善心理健康和哮喘控制的自我评价(无改善、略有改善和明显改善)。

表1 心理药物的种类及剂量

Tab 1 Types and dosages of psychotropic medications

Pharmacological class	Medications	Dosage (mg/d)
Selective serotonin reuptake inhibitors (SSRIs)	Escitalopram	2.5-10
Noradrenergic and specific serotonergic antidepressants (NaSSAs)	Mirtazapine	5-15
Serotonin antagonist and reuptake inhibitors (SARIs)	Trazodone	12.5-50
Benzodiazepines (BZDs)	Clonazepam	0.5-2
Benzodiazepines (BZDs)	Alprazolam	0.2-0.8
Atypical antipsychotics	Aripiprazole	2.5-10
Typical antipsychotics	Sulpiride	50-200
Fixed-dose combination	Deanxit	0.5 (Flupentixol), 10 (Melitracen)

统计学分析 利用 R 软件(4.3.2 版本)和 Graphpad prism Version 9 进行统计分析。正态分布的定量资料用 $\bar{x} \pm s$ 表示,偏态分布的定量资料用 $M(P_{25}, P_{75})$ 表示;定性资料用频数(n)和百分比($\%$)表示。两样本定量资料比较采用 Wilcoxon 秩和检验,两样本定性资料比较采用 χ^2 检验。对各候选变量(包括哮喘基本疾病信息、控制情况、肺功能、FeNO、过敏性合并症等)进行单因素 Logistic 回归分析。筛选 $P < 0.1$ 的变量,纳入社会人口学特征(性别、年龄、婚姻和教育情况)、BMI,建立多因素 Logistic 回归分析模型。对多因素模型中的变量进行共线性诊断,结果显示所有变量容忍度 > 0.1 、VIF < 5 ,提示无明显多重共线性。采用线性混合效应模型分析干预前

后 ACT、miniAQLQ、PHQ-9 和 GAD-7 评分变化,并纳入社会人口学特征、BMI 和过敏性合并症控制混杂因素。 $P < 0.05$ 为差异有统计学意义。

结 果

患者一般情况 本研究共纳入 231 例哮喘患者,其中男性 105 例,女性 126 例,平均年龄 40.36 岁,哮喘病程平均 9.57 年。16 例(6.93%)仅合并抑郁症状,28 例(12.12%)仅合并焦虑症状,72 例(31.17%)同时合并焦虑和抑郁症状。各组患者的年龄、性别、婚姻状况、教育程度、BMI、哮喘病程、哮喘治疗分级情况见表 2。

表 2 哮喘患者的基本信息及焦虑、抑郁症状的患病情况

Tab 2 Basic characteristics and prevalence of anxiety and depression among patients with asthma [$\bar{x} \pm s, n(\%)$ or $M(P_{25}, P_{75})$]

Characteristic	Sample size (n)	Overall ($n=231$)	None ($n=115$)	Depression ($n=16$)	Anxiety ($n=28$)	Depression and anxiety ($n=72$)
Age (y)	231	40.36 \pm 15.54	43.69 \pm 16.14	42.38 \pm 16.37	38.29 \pm 13.54	35.40 \pm 13.86
Gender	231					
Male		105 (45.45)	58 (50.43)	3 (18.75)	10 (35.71)	34 (47.22)
Female		126 (54.55)	57 (49.57)	13 (81.25)	18 (64.29)	38 (52.78)
Marital status	231					
Single		78 (33.77)	29 (25.22)	6 (37.50)	8 (28.57)	35 (48.61)
Married		148 (64.07)	83 (72.17)	9 (56.25)	20 (71.43)	36 (50.00)
Widowed/divorced		5 (2.16)	3 (2.61)	1 (6.25)	0 (0)	1 (1.39)
Education level	231					
Primary		7 (3.03)	5 (4.35)	0 (0)	1 (3.57)	1 (1.39)
Secondary		52 (22.51)	27 (23.48)	3 (18.75)	8 (28.57)	14 (19.44)
College and above		172 (74.46)	83 (72.17)	13 (81.25)	19 (67.86)	57 (79.17)
BMI (kg/m ²)	217					
Underweight (< 18.5)		17 (7.83)	5 (4.67)	3 (20.00)	0 (0)	9 (13.24)
Normal weight [$18.5-24$)		108 (49.77)	53 (49.53)	7 (46.67)	15 (55.56)	33 (48.53)
Overweight [$24-28$)		70 (32.26)	38 (35.51)	4 (26.67)	9 (33.33)	19 (27.94)
Obese (> 28)		22 (10.14)	11 (10.28)	1 (6.67)	3 (11.11)	7 (10.29)
Asthma duration (y)	210	4.00 (1.50, 10.00)	2.00 (1.00, 5.00)	5.75 (1.63, 10.00)	6.00 (1.13, 20.00)	4.00 (1.50, 10.00)
Asthma treatment steps	226					
GINA 1-2		22 (9.73)	14 (12.28)	2 (13.33)	3 (10.71)	3 (4.35)
GINA 3		77 (34.07)	39 (34.21)	5 (33.33)	9 (32.14)	24 (34.78)
GINA 4		71 (31.42)	33 (28.95)	3 (20.00)	9 (32.14)	26 (37.68)
GINA 5		56 (24.78)	28 (24.56)	5 (33.33)	7 (25.00)	16 (23.19)

合并焦虑、抑郁症状的哮喘患者的社会人口学和哮喘疾病特征 231 例哮喘患者中,相比于无抑郁症状的患者,88 例(38.10%)合并抑郁症状的患者更年轻($P=0.003$)、未婚居多($P=0.003$)、体重偏轻

($P=0.037$),而两组在性别、教育程度上差异均无统计学意义(表 3);相比于无焦虑症状的患者,100 例(43.29%)合并焦虑症状的患者更年轻($P < 0.001$)、未婚居多($P=0.021$),而两组在性别、教育程度、

BMI等方面差异均无统计学意义(表3)。

进一步分析哮喘患者的疾病特征,相较于无抑郁、焦虑症状的患者,合并抑郁、焦虑症状的患者胸闷症状更明显(抑郁: $P=0.007$;焦虑: $P=0.002$),但

两组在哮喘病程、GINA治疗分级、哮喘症状数量、肺功能、气道可逆性、FeNO等方面差异均无统计学意义(表3)。

表3 合并焦虑、抑郁症状的哮喘患者的社会人口学和疾病特征

Tab 3 Sociodemographic and disease characteristics of patients with asthma combined with anxiety or depression

Characteristic	Depression			Anxiety		
	Without depression (n=143)	With depression (n=88)	P	Without anxiety (n=131)	With anxiety (n=100)	P
Age (y)	42.63 ± 15.77	36.67 ± 14.50	0.003	43.53 ± 16.11	36.21 ± 13.77	<0.001
Gender			0.414			0.698
Male	68 (47.55)	37 (42.05)		61 (46.56)	44 (44.00)	
Female	75 (52.45)	51 (57.95)		70 (53.44)	56 (56.00)	
Marital status			0.003			0.021
Single	37 (25.87)	41 (46.59)		35 (26.72)	43 (43.00)	
Married	103 (72.03)	45 (51.14)		92 (70.23)	56 (56.00)	
Widowed/divorced	3 (2.10)	2 (2.27)		4 (3.05)	1 (1.00)	
Education level			0.261			0.829
Primary	6 (4.20)	1 (1.14)		5 (3.82)	2 (2.00)	
Secondary	35 (24.48)	17 (19.32)		30 (22.90)	22 (22.00)	
College and above	102 (71.33)	70 (79.55)		96 (73.28)	76 (76.00)	
BMI (kg/m ²) ^a			0.037			0.794
Underweight (<18.5)	5 (3.73)	12 (14.46)		8 (6.56)	9 (9.47)	
Normal weight [18.5–24)	68 (50.75)	40 (48.19)		60 (49.18)	48 (50.53)	
Overweight [24–28)	47 (35.07)	23 (27.71)		42 (34.43)	28 (29.47)	
Obese (>28)	14 (10.45)	8 (9.64)		12 (9.84)	10 (10.53)	
Asthma duration (y)	4.00 (1.50, 10.00)	5.00 (1.00, 20.00)	0.562	4.00 (1.43, 10.00)	6.00 (1.50, 20.00)	0.141
Asthma treatment steps ^b			0.496			0.327
GINA 1–2	17 (11.97)	5 (5.95)		16 (12.40)	6 (6.19)	
GINA 3	48 (33.80)	29 (34.52)		44 (34.11)	33 (34.02)	
GINA 4	42 (29.58)	29 (34.52)		36 (27.91)	35 (36.08)	
GINA 5	35 (24.65)	21 (25.00)		33 (25.58)	23 (23.71)	
Asthma symptoms	1.85 ± 0.77	2.00 ± 0.77	0.136	1.83 ± 0.76	2.01 ± 0.78	0.072
Wheeze	106 (74.13)	62 (70.45)	0.543	97 (74.05)	71 (71.00)	0.607
Cough	82 (57.34)	51 (57.95)	0.927	75 (57.25)	58 (58.00)	0.909
Chest tightness	77 (53.85)	63 (71.59)	0.007	68 (51.91)	72 (72.00)	0.002
Spirometry						
Pre-bronchodilator FEV ₁ (L)	2.82 ± 1.02	2.94 ± 1.07	0.422	2.77 ± 1.00	3.00 ± 1.09	0.109
Pre-bronchodilator FEV ₁ %pred (%)	88.13 ± 21.89	88.49 ± 19.73	0.990	86.88 ± 21.27	90.17 ± 20.82	0.326
Pre-bronchodilator FVC (L)	3.69 ± 1.05	3.80 ± 1.19	0.538	3.61 ± 1.04	3.90 ± 1.16	0.057
Pre-bronchodilator FEV ₁ /FVC (%)	75.33 ± 12.28	76.17 ± 12.61	0.565	75.47 ± 12.08	75.86 ± 12.85	0.601
Bronchodilator response						
FEV ₁ improvement (L)	0.11 ± 0.14	0.13 ± 0.17	0.481	0.10 ± 0.14	0.14 ± 0.17	0.250
FEV ₁ %pred improvement	3.65 ± 4.55	4.55 ± 5.19	0.381	3.50 ± 4.52	4.61 ± 5.11	0.196
FeNO (ppb)	45.14 ± 38.46	38.39 ± 31.65	0.151	45.94 ± 38.70	38.15 ± 32.06	0.051

^aThe sample size of BMI is 217, including 134 cases without depression and 83 cases with depression, or 122 cases without anxiety and 95 cases with anxiety. ^bThe sample size of asthma treatment steps is 226, including 142 cases without depression and 84 cases with depression or 129 cases without anxiety and 97 cases with anxiety. FEV₁: Forced expiratory volume in first second; FEV₁%pred: Percentage of predicted FEV₁; FVC: Forced vital capacity; FeNO: Fractional exhaled nitric oxide (1 ppb=1 μg/L).

合并焦虑、抑郁症状的患者哮喘急性发作和控制情况如表4所示,相较于无抑郁、焦虑症状的患者,合并抑郁、焦虑症状的哮喘患者在过去3个月内急性发作次数显著增加(抑郁: $P=0.020$;焦虑: $P<0.001$),

ACT评分(抑郁: $P<0.001$;焦虑: $P<0.001$)更低,哮喘控制不佳人群比例显著增加(抑郁: $P<0.001$;焦虑: $P<0.001$),miniAQLQ评分更低(抑郁: $P<0.001$;焦虑: $P<0.001$),提示患者的哮喘相关生活质量不佳。

表4 合并焦虑、抑郁症状的哮喘患者哮喘控制情况和过敏性合并症

Tab 4 Asthma control and allergic comorbidities of patients with anxiety and depression [$\bar{x} \pm s$ or $n(\%)$]

Characteristic	Depression			Anxiety		
	Without depression ($n=143$)	With depression ($n=88$)	P	Without anxiety ($n=131$)	With anxiety ($n=100$)	P
Asthma attack in past 3 mo	0.81 ± 1.60	1.79 ± 3.92	0.020	0.59 ± 1.28	1.97 ± 3.79	<0.001
ACT scores	20.28 ± 3.68	16.84 ± 4.64	<0.001	20.34 ± 3.77	17.18 ± 4.52	<0.001
Asthma control			<0.001			<0.001
Well	94 (65.73)	32 (36.36)		87 (66.41)	39 (39.00)	
Not well	33 (23.08)	22 (25.00)		28 (21.37)	27 (27.00)	
Very poorly	16 (11.19)	34 (38.64)		16 (12.21)	34 (34.00)	
MiniAQLQ scores	76.25 ± 15.83	61.38 ± 14.12	<0.001	75.76 ± 16.05	63.81 ± 15.37	<0.001
Allergic comorbidities	0.99 ± 0.77	1.26 ± 0.96	0.040	0.92 ± 0.72	1.32 ± 0.96	0.001
Rhinitis	100 (69.93)	68 (77.27)	0.224	88 (67.18)	80 (80.00)	0.030
Nasosinusitis	13 (9.09)	7 (7.95)	0.766	8 (6.11)	12 (12.00)	0.115
Atopic dermatitis	15 (10.49)	15 (17.05)	0.150	12 (9.16)	18 (18.00)	0.048
Urticaria	5 (3.50)	10 (11.36)	0.018	3 (2.29)	12 (12.00)	0.003
Conjunctivitis	6 (4.20)	11 (12.50)	0.019	7 (5.34)	10 (10.00)	0.179

ACT: Asthma Control Test; miniAQLQ: Mini Asthma Quality of Life Questionnaire.

经过单因素 Logistic 回归分析和共线性检验,发现焦虑、抑郁症状与哮喘急性发作风险增加显著相关(焦虑:OR=4.30, 95%CI: 1.78~10.38, $P<0.001$;抑郁:OR=1.22, 95%CI: 1.08~1.61, $P=$

0.003);多因素 Logistic 回归分析,发现焦虑、抑郁症状也是哮喘控制不佳的危险因素(焦虑:OR=1.93, 95%CI: 1.03~3.63, $P=0.040$;抑郁:OR=3.77, 95%CI: 2.01~7.19, $P<0.001$)(表5)。

表5 哮喘患者焦虑、抑郁症状的多因素 Logistic 回归分析

Tab 5 Multivariate Logistic regression analysis of anxiety and depression in patients with asthma

Factors	Depression		Anxiety	
	OR (95%CI)	P	OR (95%CI)	P
Asthma attack	1.22 (1.08-1.61)	0.003	4.30 (1.78-10.38)	<0.001
Poor asthma control	3.77 (2.01-7.19)	<0.001	1.93 (1.03-3.63)	0.040
Allergic comorbidities	1.42 (0.91-2.21)	0.128	1.80 (1.15-2.82)	0.010
Rhinitis	1.65 (0.85-3.32)	0.150	2.28 (1.18-4.56)	0.017
Nasosinusitis	0.95 (0.32-2.60)	0.912	2.55 (0.96-7.14)	0.064
Atopic dermatitis	1.78 (0.76-4.15)	0.197	2.28 (0.99-5.41)	0.055
Urticaria	5.72 (1.78-20.4)	0.004	5.82 (1.79-26.1)	0.008
Conjunctivitis	3.62 (1.20-11.7)	0.024	1.98 (0.67-6.03)	0.218

合并焦虑、抑郁症状的哮喘患者的过敏性合并症情况 过敏症状可表现在全身多个系统,哮喘患者往往合并至少一种过敏性疾病。如表4所示,相较于无抑郁、焦虑症状的患者,合并抑郁、焦虑症状

的患者过敏性合并症数量更多(抑郁: $P=0.04$;焦虑: $P=0.001$)。其中,合并抑郁症状的患者患荨麻疹($P=0.018$)、结膜炎($P=0.019$)的比例更高;合并焦虑症状的患者患鼻炎($P=0.03$)、过敏性皮炎($P=$

0.048)、荨麻疹($P=0.003$)的比例更高,其余过敏性合并症则无明显差异(表4)。

将焦虑、抑郁症状作为因变量,进行多因素 Logistic 回归分析。如表5所示,与无过敏性合并症的患者相比,合并过敏性疾病的哮喘患者出现焦虑症状的风险显著增加($OR=1.80, 95\%CI: 1.15\sim 2.82, P=0.010$),而两组抑郁症状的风险差异无统计学意义($OR=1.42, 95\%CI: 0.91\sim 2.21, P=0.128$)。进一步探索过敏性合并症与焦虑、抑郁症状的关联发现,相较于无对应合并症的患者,合并荨麻疹、结膜炎的哮喘患者出现抑郁症状的风险更高(荨麻疹: $OR=5.72, 95\%CI: 1.78\sim 20.4, P=0.004$;结膜炎: $OR=3.62, 95\%CI: 1.20\sim 11.7, P=0.024$),合并鼻炎、荨麻疹的哮喘患者出现焦虑症状的风险更高(鼻炎: $OR=2.28, 95\%CI: 1.18\sim 4.56, P=0.017$;荨麻疹: $OR=5.82, 95\%CI: 1.79\sim 26.10, P=0.008$)。

哮喘患者心理干预前后焦虑、抑郁症状和哮喘改善情况 52例哮喘患者于变态反应多学科门诊接受了心理医学科医师提供的个体化治疗,包括药物和非药物干预。患者平均年龄33.21岁,男性占50%,大学及以上学历占80.77%(表6)。其中,21例患者仅接受心理行为干预,31例患者则联合药物治疗和心理行为干预。利用MMAS-4评估患者用药依从性,31例患者中12例依从性高,14例依从性中等,5例依从性不佳。52例患者接受心理干预后,20例认为心理状况改善明显,17例认为略有改善,15例认为无改善;25例认为哮喘控制改善明显,14例认为略有改善,13例认为无改善。52例患者在心理干预前后的ACT评分分别为 16.73 ± 5.23 和 19.06 ± 4.60 , miniAQLQ评分分别为 66.02 ± 17.30 和 72.40 ± 14.78 , PHQ-9评分分别为 7.94 ± 6.13 和 6.75 ± 5.49 , GAD-7评分分别为 9.46 ± 5.20 和 7.08 ± 4.69 。仅接受心理行为干预和联合药物治疗的两组患者差异无统计学意义(表7)。利用线性混合效应模型,在控制社会人口学因素(如性别、年龄、婚姻、教育程度)、BMI、过敏性合并症数量后,干预前后ACT评分($\beta=2.29, 95\%CI: 1.33\sim 3.26, P<0.001$)、miniAQLQ评分($\beta=6.16, 95\%CI: 2.61\sim 9.70, P=0.001$), PHQ-9评分($\beta=-1.14, 95\%CI: -1.82\sim -0.45, P=0.002$)和GAD-7评分($\beta=-2.33, 95\%CI: -3.15\sim -1.51, P<0.001$)的均有显著改善(图1)。

表6 心理干预组与非干预组哮喘患者的社会人口学及临床特征比较

Tab 6 Comparison of demographic and clinical characteristics between patients with asthma receiving or not receiving psychological interventions [$\bar{x}\pm s$ or $n(\%)$]

Characteristic	Without psychological interventions ($n=179$)	With psychological interventions ($n=52$)
Age (y) ^a	42.44 ± 15.88	33.21 ± 11.92
Gender		
Male	79 (44.13)	26 (50.00)
Female	100 (55.87)	26 (50.00)
Marital status		
Single	58 (32.40)	20 (38.46)
Married	116 (64.80)	32 (61.54)
Widowed/divorced	5 (2.79)	0 (0)
Education level		
Primary	6 (3.35)	1 (1.92)
Secondary	43 (24.02)	9 (17.31)
College and above	130 (72.63)	42 (80.77)
BMI (kg/m ²) ^b		
Underweight (<18.5)	12 (7.14)	5 (10.20)
Normal weight [18.5–24)	83 (49.40)	25 (51.02)
Overweight [24–28)	60 (35.71)	10 (20.41)
Obese (>28)	13 (7.74)	9 (18.37)
Asthma duration (y)	9.68 ± 12.89	9.21 ± 11.33
Asthma treatment steps ^c		
GINA 1–2	20 (11.49)	2 (3.85)
GINA 3	61 (35.06)	16 (30.77)
GINA 4	51 (29.31)	20 (38.46)
GINA 5	42 (24.14)	14 (26.92)
Asthma control		
Well	105 (58.66)	21 (40.38)
Not well	40 (22.35)	15 (28.85)
Very poorly	34 (18.99)	16 (30.77)
Asthma attack in past 3 mo	0.90 ± 1.84	1.26 ± 3.49
Number of allergic comorbidities ^a	0.98 ± 0.81	1.48 ± 0.99

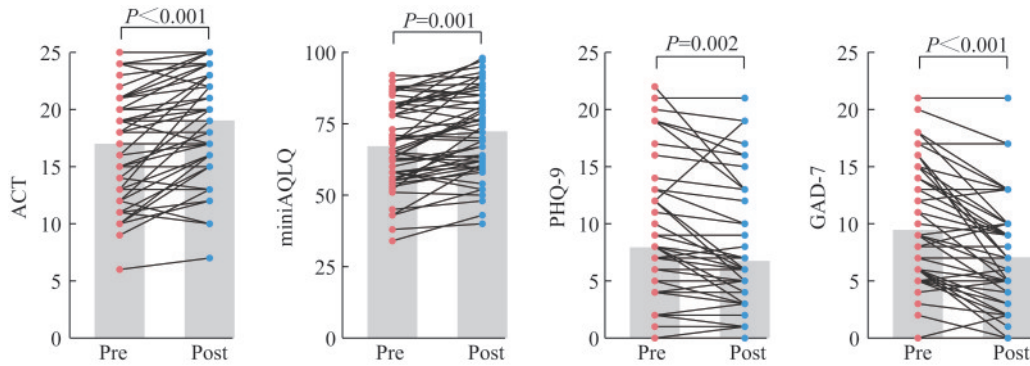
^a $P<0.001$. ^bThe sample size of BMI is 217, including 168 cases without psychological interventions and 49 cases with psychological interventions. ^cThe sample size of asthma treatment steps is 226, including 174 cases without psychological interventions and 42 cases with psychological interventions.

表7 52例接受心理干预的哮喘患者的基本信息、心理状态及哮喘改善情况

Tab 7 Basic information and improvement in psychological and asthma status among 52 patients with asthma receiving psychological interventions [n(%) or $\bar{x} \pm s$]

Characteristic	Total (n=52)	Psychological interventions		P
		Only psychobehavioral interventions (n=21)	Combined psychological interventions (n=31)	
Age (y)	33.21 ± 11.92	32.81 ± 12.78	33.48 ± 11.52	0.859
Gender				0.158
Male	26 (50.00)	8 (38.10)	18 (58.06)	
Female	26 (50.00)	13 (61.90)	13 (41.94)	
Marital status				0.772
Single	20 (38.46)	9 (42.86)	11 (35.48)	
Married	32 (61.54)	12 (57.14)	20 (64.52)	
Widowed/divorced	0 (0)	0 (0)	0 (0)	
Education level				0.567
Primary	1 (1.92)	0 (0)	1 (3.23)	
Secondary	9 (17.31)	5 (23.81)	4 (12.90)	
College and above	42 (80.77)	16 (76.19)	26 (83.87)	
BMI (kg/m ²) ^a				0.313
Underweight (<18.5)	5 (10.20)	1 (5.26)	4 (13.33)	
Normal weight [18.5–24)	25 (51.02)	9 (47.37)	16 (53.33)	
Overweight [24–28)	10 (20.41)	3 (15.79)	7 (23.33)	
Obese (>28)	9 (18.37)	6 (31.58)	3 (10.00)	
Pre-psychotherapy				
ACT	16.73 ± 5.23	17.38 ± 5.32	16.29 ± 5.21	0.443
miniAQLQ	66.02 ± 17.30	69.67 ± 16.22	63.55 ± 17.83	0.225
PHQ-9	7.94 ± 6.13	6.33 ± 5.99	9.03 ± 6.09	0.084
GAD-7	9.46 ± 5.20	7.67 ± 5.00	10.68 ± 5.04	0.056
Post-psychotherapy				
ACT	19.06 ± 4.60	19.33 ± 5.29	18.87 ± 4.15	0.495
miniAQLQ	72.40 ± 14.78	74.00 ± 14.73	71.32 ± 14.95	0.520
PHQ-9	6.75 ± 5.49	5.81 ± 5.89	7.39 ± 5.21	0.169
GAD-7	7.08 ± 4.69	5.29 ± 4.03	8.29 ± 4.78	0.052
Self-reported improvement				
Mental health				0.378
No improvement	15 (28.85)	8 (38.10)	7 (22.58)	
Mild improvement	17 (32.69)	7 (33.33)	10 (32.26)	
Significant improvement	20 (38.46)	6 (28.57)	14 (45.16)	
Asthma				0.485
No improvement	13 (25.00)	6 (28.57)	7 (22.58)	
Mild improvement	14 (26.92)	7 (33.33)	7 (22.58)	
Significant improvement	25 (48.08)	8 (38.10)	17 (54.84)	

^aThe sample size of BMI is 49, including 19 cases receiving psychobehavioral interventions and 30 cases receiving combination interventions. ACT: Asthma Control Test; miniAQLQ: Mini Asthma Quality of Life Questionnaire; PHQ-9: Patient Health Questionnaire-9; GAD-7: General Anxiety Disorder-7.



ACT: Asthma Control Test; miniAQLQ: Mini Asthma Quality of Life Questionnaire; PHQ-9: Patient Health Questionnaire-9; GAD-7: General Anxiety Disorder-7; Pre: Pre-psychotherapy; Post: Post-psychotherapy.

图1 52例哮喘患者在接受心理干预前后ACT、miniAQLQ、PHQ-9和GAD-7的改善情况

Fig 1 Changes in ACT, miniAQLQ, PHQ-9 and GAD-7 scores before and after psychotherapy in 52 patients with asthma

讨论

本研究显示,年轻、未婚、合并其他过敏性疾病的哮喘患者更易出现焦虑、抑郁症状。相较于无焦虑、抑郁症状的患者,合并焦虑、抑郁症状的患者急性发作和哮喘控制不佳的风险更高。合并过敏性疾病与更高的焦虑症状风险密切相关,个体化心理干预对哮喘患者的心理健康和哮喘控制均有改善作用。

哮喘患者中常见合并焦虑、抑郁症状。一项涉及60个国家245 404例受试者的研究结果显示,哮喘患者合并抑郁的患病率达18.1%(95%CI: 15.9%~20.3%)^[7],另一项纳入19项研究共106 813例受试者的meta分析结果显示,哮喘患者中焦虑的患病率达32%(95%CI: 22%~43%)^[4]。哮喘患者合并焦虑、抑郁的风险显著高于健康对照^[4,8]。另一方面,焦虑、抑郁不利于哮喘患者的疾病控制,通常表现为急性发作更频繁^[9]、生活质量更低^[10]、治疗依从性更差^[11]和生物制剂反应性更差^[12]。因此,焦虑、抑郁等心理因素在哮喘控制中既是哮喘疾病负担的结果,又是病情恶化的驱动因素。此外,有别于既往局限于过敏性鼻炎、特应性皮炎、食物过敏等单一过敏性疾病的研究^[13-16],本研究立足于过敏为一类全身性疾病的整体观念,探讨了过敏性合并症对哮喘患者心理健康的影响。我们将“过敏性合并症数量”作为关键的量化指标,揭示了过敏负担与焦虑、抑郁风险之间的相关性,为理解过敏与焦虑、抑郁的关系提供了新的证据。

哮喘与焦虑、抑郁密切相关的生物学机制仍未完全阐明。研究发现焦虑、抑郁和哮喘之间存在遗传易感性^[17-18]。除了遗传因素,哮喘的过敏性炎症会引发大脑结构与功能的改变^[19]。研究发现哮喘模型中前额叶皮层、杏仁核等与情绪密切相关的脑区神经元活性增加^[20]。欧洲U-BIOPRED队列研究发现,全身性炎症是哮喘与焦虑、抑郁共病的重要病理生理基础^[21]。哮喘患者中异常活化的炎症因子可通过血脑屏障直接或激活传入神经,间接引起大脑炎症。在哮喘小鼠模型中发现脑内TNF- α 、IL-1 β 等炎症因子水平升高以及小胶质细胞的激活,会诱导神经元损伤和死亡^[22]。另一方面,应激和心理压力可增加哮喘小鼠模型的气道高反应性和气道炎症,降低糖皮质激素敏感性^[23]。心理压力诱导的神经肽可加重哮喘气道炎症反应^[24]。因此,焦虑、抑郁与哮喘存在密切的双向联系,其相互作用机制可能涉及遗传、神经、免疫及炎症等多个层面。提示我们在临床管理中应将心理评估和干预纳入哮喘的综合治疗方案中,从而为患者提供更为全面和有效的治疗策略。

焦虑、抑郁与哮喘控制密切相关,给予合并焦虑、抑郁的哮喘患者必要的心理干预至关重要。本研究对接受心理干预的哮喘患者进行了前瞻性随访,系统评估干预后哮喘控制水平与心理健康状况的改善。前瞻性研究设计为心理干预在哮喘管理中的实际效果提供了纵向证据,也增强了研究结果在真实临床环境中的可信度与适用性。此外,与既往研究采用单一心理干预方式不同,本研究采用了个体化的综合心理干预策略,具体包括正念冥想、

腹式呼吸训练、渐进肌肉放松训练、行为激活,以及抗焦虑或抑郁药物等。尽管既往研究已发现了单一干预方式的有效性,但在真实临床场景中综合干预方案可以更全面地匹配患者复杂且共存的临床需求,具有更强的临床适用性和协同效应。研究发现抗抑郁药可以改善哮喘控制^[25]和降低口服激素用量^[26]。Andreasson等^[27]发现呼吸训练可以缓解哮喘患者的焦虑症状并提升生活质量。一项随机对照研究发现,正念减压可改善哮喘患者的临床控制和FeNO水平^[28]。Kew等^[29]综述了9项采用认知行为疗法(cognitive behavioral therapy, CBT)治疗哮喘患者的RCT研究,认为CBT治疗可改善患者的哮喘患者生活质量。综合分析青少年及成人哮喘患者采用心理行为干预的临床研究,包括认知疗法、行为疗法、CBT、放松训练等,多数研究发现心理行为干预有助于降低哮喘急性发作,改善焦虑、抑郁症状和哮喘控制^[30-32]。

心理干预可通过调节神经-免疫-内分泌轴等多重生物学通路,干预哮喘的病理生理进程。正念减压训练可特异性增强大脑功能连接,并和哮喘炎症标志物的降低密切相关^[33]。心理行为干预可抑制与威胁反应相关脑区(如杏仁核、前扣带皮层)的过度激活,并增强前额叶皮层的情绪调节与执行控制功能,从改善患者对呼吸困难的主观感知^[34]。在药物干预层面,抗抑郁药被证实具有抗炎作用^[35],其机制涉及对核因子 κ B,过氧化物酶体增殖物激活受体 γ 和Toll样受体-4等关键信号通路的抑制^[36],而这些通路在驱动哮喘气道炎症与免疫反应中同样具有重要作用。上述发现初步揭示了心理干预改善哮喘的潜在机制,但仍有待进一步的系统研究。

本研究中,心理干预对于改善哮喘症状和心理状态具有积极意义,但仍有约1/4的患者报告无显著改善。这一现象可能源于多方面因素,个体对于干预技巧的掌握程度与执行依从性存在差异。患者的疾病异质性同样会影响治疗反应性,哮喘的严重程度(如已形成不可逆的气道重塑)、合并未治疗的精神障碍(如复杂性创伤后应激障碍、惊恐发作)、持续的过敏原暴露、难以去除的社会心理应激源等也可能影响干预效果。除了采用个体化的干预管理方案,对初始治疗反应不佳的患者,可启动多维度的评估与干预方案的强化调整。

本研究的局限性在于横断面研究无法确定因

果关系,且易有混杂因素和反向因果关系的干扰;接受心理干预的患者病例数较少,可能存在选择偏倚;前瞻性研究随访时间较短,未能评估心理干预的长期依从性和疗效的维持情况。未来研究可延长随访时间,并引入基于诊断标准的结构化访谈,明确哮喘患者焦虑、抑郁的具体亚型,完善社会支持水平、压力应对方式的评估,以实现更精准的患者分层与管理。通过更大样本量的多中心随机对照试验,明确不同心理干预模式的有效性及成本效益,以优化哮喘患者的综合管理策略。

本研究着重强调在哮喘临床管理中关注患者心理健康的必要性,并发现过敏性合并症是哮喘患者焦虑情绪的重要危险因素。心理行为干预在改善哮喘控制方面所展现出的显著疗效为心身医学模式提供了有力的实证支持。联合心理医学科的变态反应多学科门诊可为过敏性疾病患者提供更加全面、精准的诊断和治疗,从而打破心理与生理之间的恶性循环。

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利益冲突声明 所有作者均声明不存在利益冲突。

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