

[doi: 10.3969/j.issn.1006-7795.2022.01.022]

· 临床研究 ·

王荣欣<sup>1\*</sup> 王晶<sup>1</sup> 胡水清<sup>2</sup>

(1. 首都医科大学宣武医院急诊科, 北京 100053; 2. 首都医科大学宣武医院消化科, 北京 100053)

**【摘要】 目的** 通过对伴有和不伴有食管外 (extra-esophageal, EE) 症状的反流性食管炎 (reflux esophagitis, RE) 患者的一般人口学资料、生活方式、饮食习惯、合并症、目前用药、焦虑、抑郁等方面的比较, 探讨 EE 症状发生的危险因素。**方法** 选取 2016 年 9 月到 2017 年 8 月于首都医科大学宣武医院消化科门诊就诊, 并于胃镜下明确诊断为 RE 的 361 例患者为研究对象, 以是否存在 EE 症状, 将其分为伴 EE 症状组和不伴 EE 症状组。采用问卷调查的方法对其进行一般人口学资料、生活方式、饮食习惯、合并症、目前用药、患者健康问卷-9 (Patient Health Questionnaire-9, PHQ-9) 抑郁量表、广泛性焦虑障碍-7 (General Anxiety Disorder-7, GAD-7) 焦虑量表、胃食管反流病量表 (Gastroesophageal Reflux Disease Questionnaire, GerdQ)、反流症状指数评分等方面的调查。**结果** 361 例 RE 患者中, 伴 EE 症状者 218 例, 以咽部异物感、反复咽喉痛及慢性咳嗽多见, 分别占 52.75%、46.79% 和 26.15%。单因素分析显示, 两组患者在低教育水平、吸烟、便秘、高体质量指数 (body mass index, BMI)、焦虑及抑郁方面, 差异存在统计学意义 ( $P < 0.05$ )。多元 Logistic 回归分析显示, 低教育水平 ( $OR: 1.646, 95\% CI: 1.049 \sim 2.572, P < 0.05$ )、吸烟 ( $OR: 2.488, 95\% CI: 2.047 \sim 3.281, P < 0.01$ )、高 BMI ( $OR: 1.067, 95\% CI: 1.004 \sim 1.135, P < 0.05$ )、抑郁 ( $OR: 1.062, 95\% CI: 1.002 \sim 1.133, P < 0.05$ ) 及焦虑 ( $OR: 1.061, 95\% CI: 1.001 \sim 1.131, P < 0.05$ ) 是 RE 患者发生 EE 症状的危险因素。**结论** RE 患者以咽部异物感、反复咽喉痛及慢性咳嗽为主要 EE 症状; 低教育水平、高 BMI、吸烟、抑郁和焦虑是 RE 患者发生 EE 症状的危险因素。

**【关键词】** 反流性食管炎; 食管外症状; 焦虑; 抑郁; 危险因素

**【中图分类号】** R57 **【文献标识码】** A

## Analysis of risk factors in patients with reflux esophagitis with extra-esophageal symptoms

Wang Rongxin<sup>1\*</sup>, Wang Jing<sup>1</sup>, Hu Shuiqing<sup>2</sup>

(1. Emergency Department, Xuanwu Hospital, Capital Medical University, Beijing 100053, China; 2. Department of Gastroenterology, Xuanwu Hospital, Capital Medical University, Beijing 100053, China)

**【Abstract】 Objective** To determine the risk factors of the reflux esophagitis (RE) with extra-esophageal (EE) symptoms by comparing general demographic information, lifestyle, eating habits, comorbidities, current medications, anxiety, depression of RE patients with and without EE symptoms. **Methods** The subjects of the study were seen in the Department of Gastroenterology, Xuanwu Hospital, Capital Medical University from September 2016 to August 2017 and were clearly diagnosed as RE under gastroscopy. There were 361 cases in total. They were divided into group with EE symptoms and group without EE symptoms. The patients were surveyed on General demographic information, lifestyle, eating habits, comorbidities, current medications, Patient Health Questionnaire-9 (PHQ-9) Depression Scale, General Anxiety Disorder-7 (GAD-7) Anxiety Scale, Gastroesophageal Reflux Disease Questionnaire (GerdQ) and Reflux Symptom Index (RSI). **Results** Among the 361 patients with RE, there were 218 patients with EE symptoms. Sensation of foreign body within the throat, recurrent sore throat and chronic cough were more common, accounting for 52.75%, 46.79% and 26.15% respectively. Univariate analysis showed that there were significant differences in low education level, smoking, constipation, high body mass index (BMI), anxiety, and depression ( $P < 0.05$ ) between two groups. Multivariate Logistic regression analysis identified that low education level ( $OR: 1.646, 95\% CI: 1.049 \sim 2.572, P < 0.05$ ), smoking ( $OR: 2.488, 95\% CI: 2.047 \sim 3.281, P < 0.01$ ), high BMI ( $OR: 1.067, 95\% CI: 1.004 \sim 1.135, P < 0.05$ ), depression ( $OR: 1.062, 95\% CI: 1.002 \sim 1.133, P < 0.05$ ), anxiety ( $OR: 1.061, 95\% CI: 1.001 \sim 1.131, P < 0.05$ ) were the risk factors of onset of EE symptoms in RE patients. **Conclusion** The main extra-esophageal symptoms of RE were sensation of foreign body within the throat and recurrent sore throat, chronic cough. Low education level, high BMI, smoking, depression and anxiety were risk factors of RE with extra-esophageal symptoms.

\* Corresponding author, E-mail: wangrongxin@sina.com

**【Key words】** reflux esophagitis; extra-esophageal symptoms; depression; anxiety; risk factors

(gastroesophageal reflux disease, GERD) [1], (reflux esophagitis, RE) GERD [2], RE 9.0% ~ 24.6%。 Barrett (Barrett's esophagus, BE), BE 0.5%, 85% [3], (extra-esophageal, EE) [1], RE EE, RE EE。

### 1 对象与方法

#### 1.1 研究对象

2016 9 2017 8 RE (Los Angeles, LA) [4], A、B、C、D [5], <18 ; ; [4]。 RE EE EE。

#### 1.2 资料收集及方法

RE , 361 。

##### 1.2.1 基础资料

( 、 、 、 、 )、 ( 、 、 、 、 )、 ( 、 、 、 、 )、 ( 、 ) [4]。

##### 1.2.2 胃食管反流量表(Gastroesophageal Reflux Disease Questionnaire, GerdQ) [6]

6 , 、 、 、 2。

、 0 ~ 18 。

##### 1.2.3 患者健康问卷-9 (Patient Health Questionnaire-9, PHQ-9) 抑郁量表

2 , 0 ~ 27 , >4 [7]。

##### 1.2.4 广泛性焦虑障碍-7 (General Anxiety Disorder-7, GAD-7) 焦虑量表

2 , 0 ~ 21 , >4 [7]。

##### 1.2.5 反流症状指数 (Reflux Symptom Index, RSI) 评分

、 、 9 RSI , RSI > 13 [8], 、 。

#### 1.3 统计学方法

SPSS 22.0 。  $\bar{x} \pm s$  ,  $t$  ;  $M(P_{25}, P_{75})$  ,  $\chi^2$  。 Logistic , (OR) 95% (CI) 。  $P < 0.05$  。

### 2 结果

#### 2.1 伴 EE 症状组患者主要的食管外症状

361 RE , EE 218 、 EE 143 。 EE 52.75%、 46.79% 26.15% , 1。

#### 2.2 两组 RE 患者胃镜下反流性食管炎分级比较

RE , EE LA-D EE , (  $P > 0.05$  ) , LA-A、LA-B、LA-C (  $P > 0.05$  ) ,

表 1 食管外症状组食管外症状的构成比  
**Tab. 1 The incidence of extra-esophageal symptoms in the group with extra-esophageal symptoms** (n = 218)

Extra-esophageal symptoms	Frequency	Composition ratio/%
Sensation of foreign body within the throat	115	52.75
Recurrent sore throat	102	46.79
Chronic cough	57	26.15
Night cough	15	6.88
Asthma	15	6.88
Clearing throat	14	6.42
Hoarse voice	12	5.50
Secretion flowing down the posterior pharyngeal wall	11	5.05

表 2 两组胃镜下反流性食管炎分级比较  
**Tab. 2 Comparison of classification of reflux esophagitis under gastroscop between two groups** n(%)

LA classification	Group with EE symptoms (n = 218)	Group without EE symptoms (n = 143)	$\chi^2$	P
LA-A	34 (15.60)	24 (16.78)	0.090	0.764
LA-B	170 (77.98)	111 (77.62)	0.006	0.936
LA-C	9 (4.13)	7 (4.90)	0.120	0.730
LA-D	5 (2.29)	1 (0.70)	0.545	0.461

LA: Los Angeles; EE: extra-esophageal.

2.3 伴有食管外症状的反流性食管炎影响因素的单因素分析

本研究采用 Logistic 回归分析, EE 患者、非 EE 患者、所 (body mass index, BMI) GerdQ, 均 EE, (P < 0.05), 详 3。

2.4 两组焦虑、抑郁的比较

GAD-7、PHQ-9 总 0~4 正值, EE EE, 间 (P < 0.05), 详 4。

2.5 RE 伴 EE 症状的影响因素的多因素分析

Logistic 定 与 RE EE 密切相 : BMI、(P 均 < 0.05), 详 5。

3 讨论

来 GERD EE 越来越引起 们 视, 日益 热点。根 无糜烂 GERD 非糜烂 (non-erosive reflux disease, NERD) RE<sup>[1]</sup>。 RE 361, 从 EE 构 来看,

, 与国 [1,9-10] 基 致。欧洲 项 [11], 13% 由 所致, Irwin [12] 项系 顾 甚 提 西 国家 85% 与 相 。 机制尚 十 , 普遍 观点 直 刺激 迷走神经 射共同作 结 果<sup>[1,13]</sup>。 [14] 黏膜 耐 天 50 次 酸刺激, 周 次 酸刺激即 造 黏膜 气 损伤, 由此 看 , , 气 酸 刺激更 敏 。直 刺激 假设认 直 作 、 气 或支气 位, 引起 、 或 。正 情况 , 完好 括 肌 (lower esophageal sphincter, LES) 上 括 肌 (upper esophageal sphincter, UES) 止 - [15-16], UES 压 - 闭 射 止 与 触<sup>[13]</sup>。 UES 作 , 国 所 同。国 [17] 压力测定 : EE RE UES 刺激时极少 收缩, 甚 扩 张, 致使 入 导致 。但 国 [14,18] : EE LES 压力 降 蠕动功 减弱, UES 压力 功 与 EE 无 。

表 3 伴有食管外症状的反流性食管炎影响因素的单因素分析

Tab. 3 Univariate analysis of risk factors of reflux esophagitis with extra-esophageal symptoms

[M(P<sub>25</sub>, P<sub>75</sub>), n(%)]

Factors	Group with EE symptoms (n = 218)	Group without EE symptoms (n = 143)	Z/ $\chi^2$	P
Age/a	54.00 (45.47, 62.00)	54.00 (40.00, 62.00)	-0.487	0.626
BMI/(kg · m <sup>-2</sup> )	24.22 (22.04, 26.33)	23.44 (21.19, 25.95)	-2.005	0.043
Male	93 (42.66)	71 (49.65)	1.702	0.193
Low education level (up to junior high school)	130 (59.63)	69 (48.25)	4.522	0.034
Lifestyle and eating habits				
Smoking (Yes)	90 (41.28)	43 (30.07)	4.667	0.031
Alcohol drinking (Yes)	45 (20.64)	30 (20.95)	0.006	0.939
Drinking strong tea (Yes)	53 (24.31)	34 (23.78)	0.014	0.907
Drinking coffee (Yes)	28 (12.84)	20 (13.99)	0.098	0.755
Preference for sweets (Yes)	103 (47.25)	71 (49.65)	0.200	0.655
Overeating (Yes)	118 (54.13)	82 (57.34)	0.361	0.548
Short interval between dinner and sleep (Yes)	113 (51.83)	79 (55.24)	0.403	0.526
Preference for spicy foods (Yes)	75 (34.40)	53 (37.06)	0.267	0.606
Preference for acidic foods (Yes)	45 (20.64)	29 (20.28)	0.007	0.934
Preference for noodles (Yes)	114 (62.29)	79 (55.24)	0.302	0.583
Preference for fried foods (Yes)	49 (22.48)	44 (30.77)	3.105	0.078
Preference for fruits (Yes)	70 (32.11)	37 (25.87)	1.610	0.205
Preference for fatty foods (Yes)	86 (39.45)	56 (39.16)	0.003	0.956
Constipation (Yes)	54 (24.77)	22 (15.38)	4.577	0.033
Sleeping on a low pillow (Yes)	95 (43.58)	64 (44.76)	0.049	0.826
Comorbidities				
Hypertension (Yes)	65 (29.82)	39 (27.27)	0.272	0.602
Ischemic heart disease (Yes)	21 (9.63)	8 (5.59)	1.906	0.168
Diabetes mellitus (Yes)	21 (9.63)	13 (9.09)	0.030	0.863
Cerebrovascular disease	8 (3.67)	5 (3.50)	0.007	0.931
Current medications (oral)				
Low				

表 5 与食管外症状相关的多因素分析  
Tab. 5 Multivariate analysis of factors associated with EE symptoms

Factors	B	Wald $\chi^2$	P	OR	95% CI	
					Lower limit	Upper limit
Low education level	0.496	4.710	0.030	1.646	1.049	2.572
Smoking	1.024	7.565	0.005	2.488	2.047	3.281
High BMI	0.065	4.349	0.037	1.067	1.004	1.135
Constipation	-0.372	1.578	0.209	0.689	0.385	1.232
Depression	0.063	4.339	0.038	1.062	1.002	1.133
Anxiety	0.062	4.328	0.039	1.061	1.001	1.131
GerdQ score	-0.074	3.441	0.064	0.928	0.858	1.004

EE: extra-esophageal; BMI: body mass index; GerdQ: Gastroesophageal Reflux Disease Questionnaire.

， 、 BMI、  
与 RE 呈正相，但与  
龄、他 无相，  
与国 [18,20] 所。另，国  
[21] 程度越 更易  
EE，但，根 LA 级，  
各级所 无，处  
建议未来 步扩 样。  
从 程度来看， EE  
影响 卫、 理解  
知 [1,9]、 理压力 从 导致  
增。 BMI RE  
EE 独立，与国  
[10,22] 致，原 与： 导  
致 LES 压力 降， BMI 导致腹 压增，引起  
LES 松弛时间延长， 增加  
；另 减少唾液  
泌，导致 腔干燥，从 引起  
适、 [10,23]。  
来、 与 RE 密切相  
[4,24]， 与无 EE 相， 与 EE  
更 密切。二 十  
清楚，：① /，由  
枢 经 影响导致 排空延迟，LES 松弛  
时间延长，增加了 端 微 误；②  
、 脑- 轴增加，诱  
经，引起、 [1,9,24]。  
综上所述，：RE  
、 BMI、 EE

，应引起 视。但 这 局限  
：①这，推 他；②  
，未考 NERD；③所  
未 测压 24 h pH 阻抗监测，无  
与 动力 间，未来值得  
步完善。

4 参考文献

[1] Durazzo M, Lupi G, Cicerchia F, et al. Extra-esophageal presentation of gastroesophageal reflux disease: 2020 update[J]. J Clin Med, 2020, 9(8): 2559.  
[2] Chang C H, Wu C P, Wang J D, et al. Alcohol and tea consumption are associated with asymptomatic erosive esophagitis in Taiwanese men[J]. Plos One, 2017, 12 (3): e0173230.  
[3] Ronkainen J, Talley N J, Storskrubb T, et al. Erosive esophagitis is a risk factor for Barrett’s esophagus: a community-based endoscopic follow-up study[J]. Am J Gastroenterol, 2011, 106(11): 1946 – 1952.  
[4] ， 晶，胡 清。  
[J]。 ， 2018, 40(9): 877 – 880, 884.  
[5] Lundell L R, Dent J, Bennett J R, et al. Endoscopic assessment of oesophagitis: clinical and functional correlates and further validation of the Los Angeles classification[J]. Gut, 1999, 45(2): 172 – 180.  
[6] Jones R, Junghard O, Dent J, et al. Development of the GerdQ, a tool for the diagnosis and management of gastro-oesophageal reflux disease in primary care[J]. Aliment Pharmacol Ther, 2009, 30(10): 1030 – 1038.  
[7] Teymoori A, Gorbunova A, Haghish F E, et al. Factorial structure and validity of depression (PHQ-9) and anxiety (GAD-7) scales after traumatic brain injury[J]. J Clin Med, 2020, 9(3): 873.  
[8] Włodarczyk E, Miśkiewicz B, Szkiełkowska A, et al. The use

- of RSI and RFS questionnaires in the Polish language version[J]. *Otolaryngol Pol*, 2018, 73(1): 1-5.
- [9] 李成, 刘青莉. GERD 伴发食管外症状危险因素及临床定量预测价值研究[J]. *宁夏医学杂志*, 2021, 43(7): 636-638.
- [10] 步光奎, 廖江涛. 以食管外症状为表现的老年胃食管反流病患者的临床特征及危险因素分析[J]. *河北医学*, 2021, 27(1): 136-141.
- [11] Jaspersen D, Kulig M, Labenz J, et al. Prevalence of extra-oesophageal manifestations in gastro-oesophageal reflux disease: an analysis based on the ProGERD study[J]. *Aliment Pharmacol Ther*, 2003, 17(12): 1515-1520.
- [12] Irwin R S, French C L, Chang A B, et al. Classification of cough as a symptom in adults and management algorithms: CHEST guideline and expert panel report[J]. *Chest*, 2018, 153(1): 196-209.
- [13] Ates F, Vaezi M F. Approach to the patient with presumed extra-oesophageal GERD[J]. *Best Pract Res Clin Gastroenterol*, 2013, 27(3): 415-431.
- [14] 沈玉玲, 曾庆新, 林志辉. 合并食管外症状的胃食管反流病患者的食管动力分析[J]. *中外医学研究*, 2020, 18(25): 125-127.
- [15] 苏卫仙, 代金玉, 史增辉. 反流性食管炎患者血清 CGRP 含量变化及其与胃肠激素、炎症指标的相关性[J]. *临床误诊误治*, 2019, 32(7): 48-52.
- [16] 余英, 高峰, 张杰. 反流性食管炎治疗效果与食管下段菌群构成变化的关系研究[J]. *首都医科大学学报*, 2020, 41(2): 243-248.
- [17] Babaei A, Venu M, Naini S R, et al. Impaired upper esophageal sphincter reflexes in patients with supraesophageal reflux disease[J]. *Gastroenterology*, 2015, 149(6): 1381-1391.
- [18] 杨冬, 王贞, 战秀岚, 等. 伴食管外症状的胃食管反流病患者 180 例的临床表现和食管动力学特征分析[J]. *中华消化杂志*, 2021, 41(2): 94-99.
- [19] Stein M R. Possible mechanisms of influence of esophageal acid on airway hyperresponsiveness[J]. *Am J Med*, 2003, 115(Suppl 3A): 55S-59S.
- [20] Kim S Y, Jung H K, Lim J, et al. Gender specific differences in prevalence and risk factors for gastro-oesophageal reflux disease[J]. *J Korean Med Sci*, 2019, 34(21): e158.
- [21] Schlottmann F, Andolfi C, Herbella F A, et al. GERD: presence and size of hiatal hernia influence clinical presentation, esophageal function, reflux profile, and degree of mucosal injury[J]. *Am Surg*, 2018, 84(6): 978-982.
- [22] Spantideas N, Drosou E, Bougea A, et al. Laryngopharyngeal reflux disease in the Greek general population, prevalence and risk factors[J]. *BMC Ear Nose Throat Disord*, 2015, 15: 7.
- [23] Kurin M, Fass R. Management of gastroesophageal reflux disease in the elderly patient[J]. *Drugs Aging*, 2019, 36(12): 1073-1081.
- [24] Wang R X, Wang J, Hu S Q. Study on the relationship of depression, anxiety, lifestyle and eating habits with the severity of reflux esophagitis[J]. *BMC Gastroenterol*, 2021, 21(1): 127.

(收稿日期:2021-09-04)

编辑 孙渊超