

河南省林州市食管鳞癌及癌前病变的影响因素研究

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摘要:[目的]探讨河南省林州市食管鳞癌及癌前病变的影响因素。[方法]按照性别、年龄进行1:1:1匹配的原则,选取2019年5~10月在林州市食管癌医院就诊的新发食管鳞癌患者、新发中重度食管鳞状上皮异型增生患者和正常对照匹配成33个组区作为研究对象。对入组的研究对象进行问卷调查,收集其人口学、生活方式等信息,采用多元有序Logistic回归对食管鳞癌及癌前病变的影响因素进行统计学分析。[结果]单因素分析结果显示,教育程度,饮用水来源,吸烟,饮酒,饮茶,食用西兰花、大蒜、酸菜、烟熏制品,劳动强度,消化道疾病史,食管癌家族史与食管鳞癌及癌前病变发生有关($P<0.05$)。多元有序Logistic回归结果显示,教育程度(小学:OR=2.128,95%CI:1.116~3.187;中学及以上:OR=1.960,95%CI:1.080~2.759),饮用浅层地下水、井水(OR=3.595,95%CI:1.051~7.130),现在吸烟(OR=2.027,95%CI:1.435~5.193),经常食用酸菜(OR=2.520,95%CI:1.030~4.498),经常食用烟熏制品(OR=1.312,95%CI:1.089~1.739),有消化道疾病史(OR=2.277,95%CI:1.038~2.828)是食管鳞癌及癌前病变的独立危险因素,而经常食用西兰花(OR=0.520,95%CI:0.031~0.855)是独立保护因素。[结论]在林州市,生活方式、饮食习惯和消化道病史均可影响食管鳞癌及癌前病变的发生,有其地域特点,应针对相关影响因素采取相应的预防措施。

关键词:食管鳞癌;癌前病变;影响因素;多元有序 Logistic 回归;河南

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Risk Factors of Esophageal Squamous Cell Carcinoma and Precancerous Lesions in Linzhou, Henan

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Abstract:[Purpose] To investigate the risk factors of esophageal squamous cell carcinoma and its precancerous lesions among Linzhou residents. [Methods] From May to October 2019, 33 esophageal squamous cell carcinoma cases, 33 moderate or severe esophageal squamous dysplasia cases and 33 healthy controls were selected as the subjects of study according to the principle of with gender and age matched. Questionnaire survey was carried out to collect the demographic and lifestyle information of the subjects. The multivariate ordinal Logistic regression analysis was used to analyze the independent risk factors of esophageal squamous cell carcinoma and its precancerous lesions. [Results] The univariate analysis showed that esophageal squamous cell carcinoma and its precancerous lesions were significantly associated with education level, source of drinking water, smoking, alcohol and tea drinking, consumption of broccoli, garlic, pickled vegetables and smoked products, labor intensity, history of digestive tract diseases and family history of esophageal cancer ($P<0.05$). The multivariate analysis showed that education level (primary education: OR=2.128, 95%CI: 1.116~3.187; middle education and above: OR=1.960, 95%CI: 1.080~2.759), drinking shallow groundwater and well water (OR=3.595, 95%CI: 1.051~7.130), current smoking (OR=2.027, 95% CI: 1.435~5.193), frequent consumption of pickled vegetables (OR=2.520, 95% CI: 1.030~4.498), frequent consumption of smoked products (OR=1.312, 95%CI: 1.089~1.739), history of digestive tract diseases (OR=2.277, 95%CI: 1.038~2.828) were the independent risk factors of esophageal squamous cell carcinoma and its precancerous lesions, while frequent consumption of broccoli (OR=0.520, 95%CI: 0.031~0.855) was the independent protective factor. [Conclusion] Lifestyle, diet and history of digestive tract diseases can affect the occurrence of esophageal squa-

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mous cell carcinoma and its precancerous lesions in Linzhou. Due to its geographical characteristics, corresponding preventive measures should be taken according to relevant risk factors.

Key words: esophageal squamous cell carcinoma; precancerous lesions; influencing factors; multivariate ordinal logistic regression analysis; Henan

食管癌是世界范围内最常见的消化道恶性肿瘤之一，近年来发病率和死亡率一直居高不下。2018年全球新发食管癌病例约为57.2万例，死亡病例约为50.8万例^[1]。其预后较差，对人类健康造成严重危害。我国是食管鳞状细胞癌发病率最高的国家，约占全世界食管鳞癌病例的53%，尤其是位于太行山脉南部的河北省磁县、河南省林州市（原林县）和山西省阳城县是食管癌高发区。目前认为食管鳞癌的发生发展是饮食和生活方式、人口学因素、环境与遗传因素等共同作用的结果，但确切病因尚未阐明^[2]。食管鳞癌自然史明确，其病变规律是在致癌因素和炎症因子作用下，由正常→食管上皮异型增生→原位癌。食管鳞状上皮异型增生作为食管癌变过程中必不可少的环节，其危险因素的探讨对高危人群尽早采取防治措施具有重要意义。本研究通过对林州市食管鳞癌及癌前病变流行病学调查数据进行分析，探讨食管鳞癌及癌前病变的影响因素，为食管鳞癌的一级预防提供理论依据。

1 资料与方法

1.1 研究人群

选取2019年5~10月在林州市食管癌医院就诊，进行消化内镜检查的人群。入组标准：食管鳞癌组：年龄为40~79岁，内镜检查诊断后经病理活检确诊为食管鳞癌的新发病例；异型增生组：内镜检查诊断后经病理活检确诊为中度或重度食管鳞状上皮异型增生的新发病例；正常对照组：经检查证实食管无异常增生的健康人群。三组按照性别、年龄进行1:1匹配，匹配原则是每个区组的食管鳞癌患者、中重度异型增生患者和正常对照性别相同，年龄相差不大于3岁。排除标准：近一年内曾服用抗生素，患有其他恶性肿瘤、心脑血管疾病、精神分裂、老年痴呆、消化性溃疡、消化道息肉以及其他重要脏器功能

不全者。本研究通过了中国医学科学院肿瘤医院伦理委员会批准，所有入组的研究对象均在被告知调查目的后表示自愿参与，并签署知情同意书。

1.2 资料收集

本研究采用问卷调查的方式，调查员采用由中国医学科学院肿瘤医院流行病学专家设计的调查表，对所有入组的研究对象进行面对面询问和填写，调查时间为内镜结果出来之后，确定研究对象符合纳入标准时。调查内容主要包括：人口学特征（性别、年龄、婚姻状况、受教育水平、家庭收入状况等）、生活方式（饮用水来源、吸烟、饮酒等）、饮食习惯（食用西兰花、大蒜、酸菜、烟熏制品等的频率）及消化道疾病史、肿瘤家族史等。同时，对研究对象进行统一体检，包括测量身高、体重、血压、心率等。

1.3 列入分析的因素

在充分考虑食管鳞癌的危险因素，并且结合林州市当地的情况下，一共有15项因素最终被纳入分析，食管鳞癌及癌前病变可能的影响因素和赋值见表1（Table 1）。

1.4 质量控制

食管鳞癌组和异型增生组都是在林州市食管癌医院经内镜检查和病理确诊的登记在册的患者，对照组是同期经内镜检查无异型增生的正常人。调查过程中如果出现语言沟通方面的障碍，当地的医护人员将予以配合，辅助其完成。已完成的调查问卷由质控人员全面核查，对于有漏项缺项和逻辑错误的问卷，24h内通过电话联系到调查对象本人，及时补充改正。调查问卷采用双人双机录入，保证结果的真实性和可靠性。

1.5 统计学处理

所有的数据用Epidata软件进行双人录入，最终建立数据库，采用SPSS 23.0软件进行数据分析。食管鳞癌及癌前病变的单因素分析采用Kruskal-Wallis H秩和检验，筛选出有统计学意义的变量后

Table 1 Influencing factors and their assignment for esophageal squamous cell carcinoma and precancerous lesions

Variable	Assignment		
	1	2	3
Education level	Primary education	Middle education and above	None
Annual family income (Yuan)	<10000	10000~50000	>50000
Source of drinking water	Shallow groundwater and well water	Deep ground water	Tap water
Smoking ^a	Current	Former	Do not smoke
Alcohol drinking ^b	Current	Former	Do not drink
Tea drinking ^c	Often	Occasionally	Do not drink
Soybean ^c	Often	Occasionally	Do not eat
Broccoli ^c	Often	Occasionally	Do not eat
Garlic ^c	Often	Occasionally	Do not eat
Pickled vegetables ^c	Often	Occasionally	Do not eat
Smoked products ^c	Often	Occasionally	Do not eat
Labor intensity ^d	High	Medium	Low
History of digestive tract diseases ^e	Yes	No	
Family history of esophageal cancer ^f	Yes	No	
Family history of gastric cardia cancer ^g	Yes	No	

Notes:^a:1.Smoked at least once a month for more than half a year;2.Smoked at least once a month, but now quit.^b:1.Drunk at least once a month for more than half a year;2.Drunk at least once a month, but now quit.^c:1.<Twice/week ;2.≥Twice/week.^d:1.Manpower, construction, decoration, mining, field work, steelmaking and transportation, etc. 2.Driving, electrician, fitter, metalworking, carpenter, etc. 3.Office work, sales, testing, assembly, maintenance, etc.^e:1.History of gastrointestinal diseases such as esophagitis, gastroenteritis, gastroduodenal ulcer, hepatitis, colitis, proctitis, gastrolesophageal reflux disease, etc.^f:1.Immediate family members (parents, children, sisters or brothers) were diagnosed with esophageal cancer.^g:1.Immediate family members(parents, children, sisters or brothers) were diagnosed with gastric cardia cancer

($P<0.05$),再进一步采用多元有序 Logistic 回归进行多因素分析,估计各个影响因素对食管鳞癌及癌前病变发病风险的比值比(odds ratio, OR)及 95% 可信区间(95% confidence interval, 95%CI), $P<0.05$ 认为差异有统计学意义。

2 结 果

2.1 研究对象的基本情况

本研究根据性别、年龄匹配原则,最终收集 33 个区组共 99 例,每个区组包含食管鳞癌患者、中重度异型增生患者和正常对照各 1 例。其中男性 19 个区组,女性 14 个区组。食管鳞癌组年龄 44~69 岁,平均(63.00 ± 5.64)岁,体重指数(boby mass index, BMI)($17.10\sim28.30$)kg/m²,平均(21.64 ± 2.96)kg/m²;异型增生组年龄 42~69 岁,平均(62.00 ± 5.65)岁,BMI($16.30\sim29.40$)kg/m²,平均(22.51 ± 2.71)kg/m²;正常对照组年龄 45~69 岁,平均(61.21 ± 6.02)岁,BMI($18.20\sim33.90$)kg/m²,平均(22.85 ± 3.51)kg/m²。

2.2 食管鳞癌及癌前病变影响因素的单因素分析

单因素分析的结果显示,教育程度,饮用水来

源,吸烟,饮酒,饮茶,食用西兰花、大蒜、酸菜、烟熏制品,劳动强度,消化道疾病史,食管癌家族史与食管癌及癌前病变发生有关($P<0.05$),然而未发现家庭年收入、食用大豆,贲门癌家族史与食管癌及癌前病变发生之间的统计学关联($P>0.05$),见表 2(Table 2)。

2.3 食管鳞癌及癌前病变影响因素的多因素分析

多因素分析的结果由表 3(Table 3)所示,以食管鳞癌及癌前病变的不同等级作为因变量(0=正常对照组,1=异型增生组,2=食管鳞癌组),以单因素分析中有统计学意义的变量作为自变量引入多元有序 Logistic 回归进行多因素分析。多因素分析的结果显示,教育程度(小学:OR=2.128,95%CI:1.116~3.187;中学及以上:OR=1.960,95%CI:1.080~2.759),饮用浅层地下水、井水(OR=3.595,95%CI:1.051~7.130),现在吸烟(OR=2.027,95%CI:1.435~5.193),经常食用酸菜(OR=2.520,95%CI:1.030~4.498),经常食用烟熏制品(OR=1.312,95%CI:1.089~1.739),有消化道疾病史(OR=2.277,95%CI:1.038~2.828)是食管鳞癌及癌前病变的独立危险因素($P<0.05$),而经常食用西兰花(OR=0.520,95%CI:0.031~0.855)是独立保护因素($P<0.05$)。

Table 2 Univariate Logistic regression analysis of influencing factors for esophageal squamous cell carcinoma and precancerous lesions

Variable	HC group	ESD group	ESCC group	H	P
Education level					
Primary education	7	8	19		
Middle education and above	22	16	10	5.763	0.046
None	4	9	4		
Annual family income(RMB)					
<10000	2	1	3		
10000~50000	15	17	20	5.024	0.081
>50000	16	10	6		
Source of drinking water					
Shallow groundwater and well water	3	4	10		
Deep ground water	19	13	1	9.776	0.032
Tap water	11	16	22		
Smoking					
Current	6	10	6		
Former	1	3	9	4.403	0.035
Do not smoke	26	20	18		
Alcohol drinking					
Current	4	7	5		
Former	1	3	9	5.526	0.019
Do not drink	28	23	19		
Tea drinking					
Often	5	3	13		
Occasionally	3	4	10	12.591	0.001
Do not drink	25	26	10		
Soybean					
Often	14	15	13		
Occasionally	19	12	16	4.921	0.085
Do not eat	0	6	4		
Broccoli					
Often	11	1	2		
Occasionally	6	9	6	20.913	0.001
Do not eat	16	23	25		
Garlic					
Often	17	18	10		
Occasionally	5	7	16	10.26	0.036
Do not eat	11	8	7		
Pickled vegetables					
Often	1	1	3		
Occasionally	1	5	12	15.097	0.001
Do not eat	31	27	18		
Smoked products					
Often	6	10	18		
Occasionally	22	20	14	11.112	0.025
Do not eat	5	3	1		
Labor intensity					
High	16	7	1		
Medium	4	3	6	4.569	0.041
Low	13	23	17		
History of digestive tract diseases					
Yes	18	15	7		
No	15	18	26	8.056	0.018
Family history of esophageal cancer					
Yes	10	7	14		
No	23	26	19	10.716	0.020
Family history of gastric cardia cancer					
Yes	5	4	2	1.367	0.242
No	28	29	31		

Notes: HC group: healthy control group; ESD group: esophageal squamous dysplasia group; ESCC group: esophageal squamous cell carcinoma group

3 讨 论

河南省林州市是全国食管癌的高发地区,其发病率是中国平均水平的5倍,是世界平均水平的10倍左右,比非洲西部地区高100倍以上。已有研究在林县营养干预试验随访人群的基础上,对林州市食管鳞癌发病的影响因素做了深入的探讨,发现本地居民、身高增加和吸烟为危险因素,而高教育水平,饮用自来水,经常食用肉类、鸡蛋和新鲜水果以及BMI增加为保护因素^[3]。食管癌变并不是单一因素作用的结果,是在多因素、多基因、多步骤的共同影响下发生的一个复杂过程,而食管鳞状上皮异型增生是这一过程中重要的中间环节,因此亟需进一步明确食管鳞癌及癌前病变的病因及发生机制,从而降低或延缓食管鳞癌的发生。

3.1 生活方式与食管鳞癌及癌前病变的关系

无论在发达地区还是在欠发达地区,吸烟都是食管鳞癌的主要危险因素。最近对52项研究进行的Meta分析显示,与非吸烟者相比,欧洲的目前吸烟者患食管鳞癌的风险增加了大约5倍,而亚洲和南美洲的风险增加了相应的3倍^[4]。另外,随着吸烟量和吸烟年限的增加,食管鳞癌的发生风险增加,具有明显的剂量反应关系。因此,虽然本研究的病例样本量相对较小,无法对吸烟作为食管癌的独立危险因素进行更明确的定量评估,但我们的结果与文献结论是一致的。烟草含有高达60多种致癌物,许多研究表明这些致癌物与食管鳞癌有关^[5-6],可能是烟草中的致癌物直接作用于食管黏膜上皮,引起正常细胞损伤和凋亡,从而导致具有增殖优势的异常细胞克隆,最终使癌基因突变和抑癌基因丢失。另一种解释可能是这些存在于烟草烟雾中的化合物及其体内代谢物可能与DNA发生共价结合,从

Table 3 Multivariate ordinal logistic regression analysis of influencing factors for esophageal squamous cell carcinoma and precancerous lesions

Variable	β	S.E.	Wald χ^2	P	OR	95%CI	
						Lower	Upper
Response variable Y							
Constant 1	2.471	0.482	12.154	<0.01			
Constant 2	3.487	0.497	22.990	<0.01			
Explanatory variables X							
Education level							
Primary education	3.301	0.759	8.936	0.003	2.128	1.116	3.187
Middle education and above	2.482	0.604	7.733	0.005	1.960	1.080	2.759
None					1.000		
Source of drinking water							
Shallow ground water and well water	2.610	0.892	3.408	0.045	3.595	1.051	7.130
Deep ground water	1.256	0.414	2.603	0.107	1.285	0.062	1.710
Tap water					1.000		
Smoking							
Current	3.179	0.738	14.890	0.027	2.027	1.435	5.193
Former	3.437	0.843	2.588	0.108	2.208	0.731	8.236
Do not smoke					1.000		
Alcohol drinking							
Current	2.061	0.988	23.911	0.340	3.853	0.114	5.281
Former	1.139	0.730	3.901	0.343	2.123	0.297	3.809
Do not drink					1.000		
Tea drinking							
Often	0.357	0.533	3.119	0.730	1.429	0.188	10.828
Occasionally	-0.934	0.921	1.028	0.311	0.393	0.065	2.391
Do not drink					1.000		
Broccoli							
Often	-0.654	0.435	0.208	0.044	0.520	0.031	0.855
Occasionally	-0.500	0.856	0.072	0.088	0.607	0.016	1.068
Do not eat					1.000		
Garlic							
Often	-0.569	0.801	0.287	0.592	0.566	0.070	4.549
Occasionally	-0.092	0.763	0.013	0.909	0.912	0.190	4.385
Do not eat					1.000		
Pickled vegetables							
Often	3.278	0.757	3.913	0.048	2.520	1.030	4.498
Occasionally	2.361	0.576	3.426	0.064	1.603	0.870	2.197
Do not eat					1.000		
Smoked products							
Often	1.670	0.375	14.780	0.029	1.312	1.089	1.739
Occasionally	-0.085	0.785	0.602	0.962	0.919	0.028	2.353
Do not eat					1.000		
Labor intensity							
High	-0.384	0.892	0.041	0.839	0.681	0.017	2.772
Medium	1.474	0.484	1.550	0.213	1.368	0.429	4.503
Low					1.000		
History of digestive tract diseases							
Yes	1.730	0.787	4.838	0.028	2.277	1.038	2.828
No					1.000		
Family history of esophageal cancer							
Yes	0.492	0.529	5.353	0.553	1.611	0.120	3.102
No					1.000		

而使关键基因突变，导致癌变^[7]。林州居民因其地域传统，大多数吸烟者都有饭后吸烟的习惯，在进食后食管黏膜处于充血的状态，此时吸烟对食管黏膜的刺激更大，食管黏膜更易受到致癌物的损伤。因此应该对当地长期吸烟的人群进行卫生健康教育，降低该人群患食管鳞癌的风险。

有研究表明，经常饮用浅层地下水及井水容易诱发食管上皮异型增生甚至食管鳞癌^[8]，这与我们的研究结果相一致。可能的原因是这些水质因为长期蓄积造成污染，往往不达标，含有如砷、铬、镍、铍、苯胺、苯并芘和其它多环芳烃等致癌物质，长期饮用这类水质就可能诱发食管癌变。还有很多学者认为深层或浅层地下水本身含有某些致癌物，即符合“水土因素致病理论假说”^[9]。认为井水中的诱变物主要作用于蚕豆根尖分生层细胞，在食管上皮鳞状细胞生长分裂过程中产生微核，导致鳞状上皮细胞的遗传物质丢失，如果长期作用会不断产生异己细胞，在免疫系统的作用下可发生高度增生代偿或炎症，最终演变为食管鳞癌。然而，是浅层地下水、井水受到污染，还是水源中本身存在某种致癌物，目前还没有定论，有待进一步讨论和研究。

3.2 饮食习惯与食管鳞癌及癌前病变的关系

本研究结果显示经常食用酸菜和烟熏制品是食管鳞癌及癌前病变的危险因素。有研究发现酸菜和烟熏制品提取物具有致突变性，其中含有很高比例的多环芳烃类、N-二甲基亚硝胺等亚硝基化合物，可能引发多种器官癌变，特别是与食管鳞癌发生呈正相关^[10]。针对中国人群膳食因素与食管癌的21项病例对照研究结果显示，食用酸菜与食管癌的OR_{合并}为1.71，烟熏制品与食管癌的OR_{合并}为2.79，在中国人群食管癌发病中的作用较强^[11]。林州当地居民的饮食习俗中历来就有喜食酸菜和熏鱼、熏肉等烟熏制品的特殊习惯，长期高盐饮食可能对食管黏膜造成慢性理化刺激，导致黏膜上皮局限或弥漫性不典型增生，从而形成食管鳞癌的癌前状态。因此，提示对该地区居民进行高盐饮食危害的宣教使人们养成健康的饮食习惯，对预防食管鳞癌及癌前病变具有积极意义。

本研究中发现，经常食用西兰花是食管鳞癌及癌前病变的保护因素。大量的抗癌活性研究已经证明，经常食用十字花科类蔬菜，如西兰花、白菜、萝卜等，可以降低人群肿瘤的发生风险，其中对肺癌、食管癌、胃癌、乳腺癌以及皮肤癌的作用最为明显^[12-14]。西兰花中最具有抗癌活性的芥子油苷是1-异硫氰酸-4-甲磺酰基丁烷，即萝卜硫素^[15]，是迄今发现的最主要的phase II(致癌因子解毒)酶诱导剂，不仅能对癌细胞起抑制作用，而且能够杀伤传统治疗方法或放射治疗无法杀死的肿瘤干细胞，因此该成分是预防食管癌等肿瘤发生的物质基础。其作用机制是诱导GST等phase II酶类的产生，从而作用于自身免疫系统，阻断致瘤物的代谢途径，阻止致瘤物进入靶细胞^[16]。另外萝卜硫素可能在癌前病变阶段或癌症形成初期使基因发生突变，一些抑制酶还具有抑癌功能，从而对致瘤物进行降解。因此随着人们健康意识提高和饮食结构调整，林州居民食用新鲜蔬菜的比例大幅度提高，对当地食管鳞癌疾病负担的改善具有促进作用。

3.3 教育程度与食管鳞癌及癌前病变的关系

本研究结果表明，教育水平越低，发生食管鳞癌的危险性就越大，与国内外很多研究结果一致，这可能是因为具有较高教育背景的人会享有较好的卫生保健和生活条件，更容易采取更健康的生活方式，如良好的饮食习惯和经常进行体育锻炼等^[17]。教育程

度不同，获取相关知识的方法和渠道也不同，教育程度越高，可能通过更多并且更科学的方式获取健康教育知识^[18]。还有研究表明食管癌发生率和人的社会经济地位呈负性相关^[19]，经济收入低、农民外出打工、居无定所者往往有较高的食管癌发生率，而教育水平高低间接反应了社会经济地位。关于不同教育程度的人群中食管鳞癌及癌前病变的发病率的差异应引起各方的注意，提示教育程度较低的人群和农民作为食管鳞癌预防的重点人群。

3.4 消化道疾病史与食管鳞癌及癌前病变的关系

本研究发现，有食管炎、胃肠炎、胃食管反流病等消化道病史的人群，其患食管鳞癌及癌前病变危险大大增加，这一结果与之前的研究结果相一致^[20-21]。食管癌变过程的相关研究结果显示，在食管上皮异型增生、原位癌和浸润癌的不同癌变阶段，炎性细胞浸润的程度是不同的，上皮细胞的转变与浸润程度具有一定的相关性^[22]，这提示消化道疾病史可能在食管癌变过程起着重要作用。机制可能是在炎性细胞的长期持续作用下，食管上皮基底膜会出现点、片状改变，继而断裂和缺失，细胞之间的黏附力下降，造成上皮细胞的异常增殖，从而出现异型增生^[23]。同时，持续性炎症能够刺激机体分泌细胞趋化因子、前列腺素等多种促炎递质，这些促炎递质能够诱发突变和促进新血管的生成，启动肿瘤的形成^[24]。另外，当发生胃食管反流时，胃内容物可反流进入食管，使食管壁对反流物的抵抗力下降，食管黏膜破损导致食管溃疡、狭窄和增生，长期刺激甚至癌变^[25-26]。

综上所述，林州市居民食管鳞癌及癌前病变的影响因素有其地域特征，应在此地区提倡戒烟，经常食用新鲜蔬菜，营养均衡，有消化道病史的人群定期健康检查，做到早诊断、早治疗。相关部门应结合本地的实际情况加大宣传和健康教育力度，持续推进食管癌早诊早治，并增加对食管上皮异型增生的重视程度。但是本研究的结果不能代表自然人群的全部情况，还需进行大样本、多中心、长周期的前瞻性队列研究来进行验证。

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