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食管癌患者术前营养风险评估及与术后吻合口瘘和住院时间的关系研究*

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摘要 目的:评估食管癌患者术前营养风险及其影响因素,并分析其与术后吻合口瘘和住院时间的关系。方法:回顾性分析2017年1月至2020年12月在合肥市第二人民医院胸外科行手术治疗的105例食管癌患者的临床资料,患者术前均完善营养风险筛查表-2002(NRS-2002)对其营养风险的评估,根据评估结果分为营养风险组(≥ 3 分,43例)和无营养风险组(< 3 分,62例),采用单因素及多因素Logistic回归分析食管癌患者术前营养风险的影响因素,比较不同术前营养风险状态患者术后吻合口瘘发生率以及住院时间的差异。结果:食管癌患者的术前营养风险较高,营养风险发生率为40.95%(43/105)。单因素分析结果显示,营养风险组年龄 ≥ 65 岁、入院体质量指数 $< 18.5 \text{ kg/m}^2$ 、术前接受过新辅助放化疗、过去1周膳食摄入不足、术前白蛋白 $< 35 \text{ g/L}$ 的患者比例高于无营养风险组($P < 0.05$)。多因素Logistic回归分析结果显示,术前接受过新辅助放化疗、过去1周膳食摄入不足、术前白蛋白 $< 35 \text{ g/L}$ 是食管癌患者术前存在营养风险的危险因素($P < 0.05$)。营养风险组术后胸腔吻合口瘘、颈部吻合口瘘发生率高于无营养风险组($P < 0.05$),住院时间长于无营养风险组($P < 0.05$)。结论:术前新辅助放化疗、过去1周膳食摄入情况、术前白蛋白水平是食管癌患者术前营养风险的影响因素,术前营养风险会增加患者术后吻合口瘘发生风险,延长患者住院时间。

关键词:食管癌;营养风险;吻合口瘘;住院时间

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Preoperative Nutritional Risk Assessment of Patients with Esophageal Cancer and its Relationship Study with Postoperative Anastomotic Fistula and Length of Hospital Stay*

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ABSTRACT Objective: To evaluate the preoperative nutritional risk of patients with esophageal cancer, and to analyze its relationship with postoperative anastomotic fistula and length of hospital stay. **Methods:** The clinical data of 105 patients with esophageal cancer who underwent surgical treatment in the Department of Thoracic Surgery, Hefei Second People's Hospital from January 2017 to December 2020 were retrospectively analyzed. All patients completed the nutritional risk assessment of the nutritional risk screening form-2002 (NRS-2002) before surgery, and they were divided into nutritional risk group (≥ 3 scores, 43 cases) and non-nutritional risk group (< 3 scores, 62 cases). Multivariate Logistic regression was used to analyze the influencing factors of preoperative nutritional risk in patients with esophageal cancer, and the differences in the incidence of postoperative anastomotic fistula and length of hospital stay in patients with different preoperative nutritional risk status were compared. **Results:** Preoperative nutritional risk was higher in patients with esophageal cancer, and the incidence of nutritional risk was 40.95% (43/105). Univariate analysis showed that the proportion of patients in nutritional risk group with age ≥ 65 years, admission body mass index $< 18.5 \text{ kg/m}^2$, preoperative neoadjuvant chemoradiotherapy, inadequate dietary intake in the past 1 week, preoperative albumin $< 35 \text{ g/L}$ were higher than those in non-nutritional risk group ($P < 0.05$). Multivariate Logistic regression analysis showed that preoperative neoadjuvant chemoradiotherapy, inadequate dietary intake in the past 1 week, and preoperative albumin $< 35 \text{ g/L}$ were the risk factors for preoperative nutritional risk in patients with esophageal cancer ($P < 0.05$). The incidence of thoracic anastomotic fistula and cervical anastomotic fistula in nutritional risk group were higher than those in non-nutritional risk group ($P < 0.05$), and the length of hospital stay was longer than that in non-nutritional risk group ($P < 0.05$). **Conclusion:** Preoperative neoadjuvant chemoradiotherapy, dietary intake in the past 1 week, and preoperative albumin level are the influencing factors for preoperative nutritional risk of patients with esophageal cancer. Higher preoperative nutritional risk would increase the risk of postoperative anastomotic fistula and prolong the length of hospital stay of patients.

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前言

食管癌是世界范围内最致命的恶性肿瘤之一,尽管近年来食管癌临床管理和治疗有所改善,但该病5年总生存率仍不足10%,食管切除术后5年存活率不超过40%^[1,2]。食管癌患者常伴有营养不良的状况,营养不良可导致预后不良,而良好的营养状况有助于减少并发症的发生,并改善手术效果和患者预后^[3,4]。食管癌患者营养不良的主要原因为肿瘤阻塞食道,引起进行性吞咽困难,长期进食困难导致能量摄入不足,无法满足基础代谢的需求^[5],营养不良同时还受到包括年龄、性别、吸烟、饮酒、家族史、经济收入、居住状态、心理状态、血红蛋白、白蛋白水平等其他因素的影响^[6-8]。但是目前尚无一致性结论,因此有必要了解影响食管癌术前营养风险的因素,本研究通过回顾性分析105例食管癌患者的临床资料,分析食管癌术前营养风险的影响因素,并观察其与患者术后吻合口瘘发生和住院时间的关系。

1 资料与方法

1.1 研究对象

回顾性分析2017年1月至2020年12月在合肥市第二人民医院胸外科行手术治疗的105例食管癌患者的临床资料,其中男81例,女24例;年龄51~73岁,平均(64.12±3.59)岁;入院体质量指数17~22 kg/m²,平均(19.35±2.05)kg/m²。纳入标准:^①经术后组织病理学检查证实为食管癌;^②均行食管癌根治术治疗,且成功完成手术;^③年龄18周岁以上。排除标准:^④既往有胃肠手术史;^⑤合并其它恶性肿瘤;^⑥急慢性胃炎,急慢性阑尾炎、消化性溃疡、功能性消化不良等;^⑦出现极度消瘦、严重贫血、卧床、生活不能自理、全身脏器衰竭等恶病质表现者。

1.2 营养风险评估

术前采用营养风险筛查表-NRS-2002(NRS-2002)^[9]评估所有患者的营养风险,该评分表从体质量指数、疾病状态(骨盆骨折或慢性病患者合并以下疾病:肝硬化、慢性阻塞性肺疾病、长期血液透析、糖尿病计1分,腹部重大手术、中风、重症肺炎、血液系统肿瘤计2分,颅脑损伤、骨髓抑制、重症患者计3分)、营养受损状态(近3个月体重减轻>5%,或近1周进食能量减少20%~50%计1分,近2个月体重减轻>5%,或近1周进食能量减少51%~75%,或BMI 18.5~20.5 kg/m²计2分,近1个月体重减轻>5%,或近1周进食能量减少76%~100%,或BMI<18.5 kg/m²计3分,否则计0分)、年龄(>70岁计1分,否则计0分)等方面进行评估,计分之和为评估总分,评分越高营养风险越高。据此将105例食管癌患者分为营养风险组(NRS-2002评分≥3分)和无营养风险组(NRS-2002评分<3分)。

1.3 临床资料收集

查看电子病历统计患者年龄、性别、入院体质量指数、吸烟史、饮酒史、合并慢性疾病(肝硬化、慢性阻塞性肺疾病、长期血液透析、糖尿病等)情况、食管癌病理类型、分化程度、病变部

位、是否接受术前新辅助放化疗、过去1周膳食摄入情况(24 h膳食调查摄入能量/总能量消耗≥1为摄入充分,<1为摄入不足^[10])、术前白蛋白水平、术后吻合口瘘发生情况、术后住院时间。

1.4 统计学分析

应用SPSS 25.00录入和分析数据。住院时间等计量资料以($\bar{x} \pm s$)表示,比较采用t检验。性别、基础疾病等计数资料以率(%)表示,比较采用 χ^2 检验。以单因素及多因素Logistic回归分析食管癌患者术前营养风险的影响因素。检验水准 $\alpha=0.05$ 。

2 结果

2.1 食管癌患者术前营养风险状况

105例食管癌患者NRS-2002评分1~4分,平均(2.65±0.49)分,其中43例(40.95%)存在营养风险(营养风险组),62例(59.05%)无营养风险(无营养风险组)。

2.2 食管癌患者术前营养风险的单因素分析

营养风险组年龄≥65岁、入院体质量指数<18.5 kg/m²、术前接受过新辅助放化疗、过去1周膳食摄入不足、术前白蛋白<35 g/L的患者比例高于无营养风险组($P<0.05$),而两组间性别、吸烟史、饮酒史、合并慢性疾病与否、病理类型、分化程度、肿瘤部位比较差异无统计学意义($P>0.05$),见表1。

2.3 食管癌患者术前营养风险的多因素Logistic回归分析

以术前是否存在营养风险为因变量(赋值:0=否,1=是),以年龄(赋值:0=<60岁,1=≥60岁)、入院体质量指数(赋值:0=≥18.5 kg/m²,1=<18.5 kg/m²)、术前新辅助放化疗(赋值:0=否,1=是)、过去1周膳食摄入情况(赋值:0=充分,1=不足)、术前白蛋白水平(赋值:0=≥35 g/L,1=<35 g/L)为自变量,建立多因素Logistic回归方程,采用ENTER法,最终分析结果得出:术前接受过新辅助放化疗、过去1周膳食摄入不足、术前白蛋白<35 g/L是食管癌患者术前存在营养风险的危险因素($P<0.05$),见表2。

2.4 营养风险组与无营养风险组术后吻合口瘘发生率和住院时间比较

营养风险组术后胸腔吻合口瘘、颈部吻合口瘘发生率高于无营养风险组($P<0.05$),住院时间长于无营养风险组($P<0.05$),见表3。

3 讨论

食管癌患者普遍存在营养不良状况,营养不良会导致呼吸肌无力,增加术后肺部感染发生风险,并引起伤口愈合不良和生活质量降低,延长患者住院时间^[11,12]。一项队列研究发现术前营养不良(体重减轻>10%)可增加食管癌患者食管切除术后的死亡率^[13],另一项回顾性研究报告称营养不良(BMI<18.5 kg/m²)的食管癌患者术后肺和其他并发症的风险增加^[14]。本次研究结果显示,105例食管癌患者中有43例术前存在营养风险,营养风险发生率为40.95%,提示食管癌患者术前营养风险

较高。因此,对于食管癌患者早期筛查营养不良,分析营养不良
的危险因素,并给予适当的营养支持在术前整体管理中十分
重要。

表 1 食管癌患者术前营养风险的单因素分析 [例(%)]

Table 1 Univariate analysis of preoperative nutritional risk in patients with esophageal cancer [n(%)]

Factors	Nutritional risk group (n=43)	Non-nutritional risk group(n=62)	χ^2	P
Age				
≥65 years	30(69.77)	25(40.32)	8.825	0.003
<65 years	13(30.23)	37(59.68)		
Gender				
Male	35(81.40)	46(74.19)	0.747	0.387
Female	8(18.60)	16(25.81)		
Admission body mass index(kg/m ²)				
≥18.5	14(32.56)	40(64.52)	10.381	0.001
<18.5	29(67.44)	22(35.48)		
Smoking history				
Yes	20(46.51)	38(61.29)	2.243	0.134
No	23(53.49)	24(38.71)		
Drinking history				
Yes	15(34.88)	28(45.16)	1.109	0.292
No	28(65.12)	34(54.84)		
Complicated with chronic diseases				
Yes	4(9.30)	11(17.74)	1.477	0.224
No	39(90.70)	51(82.26)		
Pathological type				
Squamous cell carcinoma	32(74.42)	50(80.65)	0.585	0.746
Adenocarcinoma	9(20.93)	10(16.13)		
Undifferentiated	2(4.65)	2(3.22)		
Degree of differentiation				
Low to moderate differentiation	31(72.09)	50(80.65)	1.053	0.305
Highly differentiation	12(27.91)	12(19.35)		
Tumor site				
Cervical segment and upper thoracic segment	5(11.63)	9(14.52)	0.325	0.850
Middle thoracic segment	20(46.51)	30(48.39)		
Lower thoracic segment	18(41.86)	23(37.09)		
Preoperative neoadjuvant chemoradiotherapy				
Yes	31(72.09)	30(48.39)	5.861	0.015
No	12(27.91)	32(51.61)		
Dietary intake in the past 1 week				
Sufficient	8(18.60)	34(54.84)	13.890	0.000
Inadequate	35(81.40)	28(45.16)		
Preoperative albumin(g/L)				
<35	32(74.42)	24(38.71)	13.008	0.000
≥35	11(25.58)	38(61.29)		

表 2 食管癌患者术前营养风险的多因素 Logistic 回归分析方程

Table 2 Multivariate Logistic regression analysis equation of preoperative nutritional risk in patients with esophageal cancer

Variables	β	SE	Wald x^2	OR(95%CI)	P
Age	0.241	0.227	1.127	1.273(0.816~1.986)	0.356
Admission body mass index	0.209	0.195	1.149	1.232(0.841~1.806)	0.307
Dietary intake in the past 1 week	0.712	0.185	14.812	2.038(1.418~2.929)	0.000
Preoperative neoadjuvant chemoradiotherapy	0.402	0.163	6.082	1.495(1.086~2.057)	0.001
Preoperative albumin	0.695	0.206	11.382	2.004(1.338~3.000)	0.000

表 3 营养风险组与无营养风险组术后吻合口瘘发生率和住院时间差异

Table 3 Difference of incidence of postoperative anastomotic fistula rate and length of hospital stay between nutritional risk group and non-nutritional risk group

Groups	n	Thoracic anastomotic fistula [n(%)]	Cervical anastomotic fistula [n(%)]	Length of hospital stay(d)
Nutritional risk group	43	3(6.98)	6(13.95)	12.35±3.46
Non-nutritional risk group	62	0(0.00)	1(1.62)	8.02±2.13
χ^2/t	-	4.410	6.214	7.297
P	-	0.036	0.013	0.000

营养不良多是由营养素摄入或吸收不足造成的，并导致体重减轻、身体成分改变以及较差的临床结果^[15]。本研究结果显示，营养风险组过去1周膳食摄入不足的患者比例明显高于无营养风险组，回归分析结果证实，过去1周膳食摄入不足是导致食管癌患者术前营养风险的危险因素。营养摄入减少和营养代谢改变可引起蛋白质和能量失衡，导致骨骼肌肉和脂肪组织损失，体重减轻和身体机能下降^[16]，食管癌营养摄入不足可能是由肿瘤堵塞食道，引起吞咽困难所致，加之肿瘤引起的全身炎症反应增加能量消耗，营养代谢改变，导致患者体重减轻^[17]。另外术前新辅助放化疗的副作用，如恶心、呕吐、腹泻、放射性食管炎等加速营养状况恶化，导致患者术前营养风险显著增高^[18]。白蛋白是人体血浆中最主要的蛋白质，具有维持机体营养和血浆胶体渗透压作用，血清白蛋白水平是公认的营养不良诊断指标^[19]，低白蛋白水平不仅与营养不良有关，而且与食管癌根治术后预后不良^[20]及胃癌患者预后不良有关^[21]，本研究结果支持白蛋白在食管癌患者术前营养风险评估中的价值，营养风险组血清白蛋白<35 g/L的患者比例高于无营养风险组，且血清白蛋白<35 g/L是食管癌术前营养风险的危险因素之一。

吻合口瘘是食管癌切除术后最常见和最严重的并发症之一，颈部吻合口瘘不危及患者生命，经引流即可痊愈，胸腔内吻合口瘘通常发生在手术后5-10 d，病情恶化时会导致胸膜污染和胃坏死，可导致患者死亡率升高^[22]。吻合口瘘的发生与年龄、糖尿病、手术方式、手术时间、管状胃制作、术后其他并发症、吻合方式、吻合部位张力、吻合部位继发感染、术前患者营养状况等诸多因素有关^[23,24]。本研究结果显示，营养风险组胸腔吻合口瘘、颈部吻合口瘘发生率均高于无营养风险组，住院时间长于无营养风险组，说明术前营养风险可增加食管癌患者术后胸腔、颈部吻合口瘘发生风险，并延长患者住院时间。李美端等人^[25]报道也指出术前营养不良与食管癌开胸根治术后手术部位感

染、吻合口瘘等并发症发生有关。伤口愈合需要足够的营养支持，营养素中氨基酸、矿物质、维生素、天然化合物等可靶向DNA调节转录因子、细胞因子、细胞外基质蛋白和糖胺聚糖，促使伤口愈合^[26]。营养元素参与伤口愈合的各个阶段，在炎症阶段，维生素A增强细胞因子释放，氨基酸可抑制炎症反应，维生素C则增强中性粒细胞迁移和淋巴细胞活化。增殖阶段，维生素C可促使胶原蛋白合成，氨基葡萄糖促进透明质酸的产生，维生素A促进上皮细胞分化，在重塑阶段，氨基酸和蛋白质在伤口疤痕稳定中起着关键作用^[27,28]。营养缺乏会导致伤口抗张强度降低，增加伤口感染率，阻碍伤口的正常愈合^[29,30]，延长住院时间。

综上，食管癌患者术前营养风险发生率高，术前接受过新辅助放化疗、过去1周膳食摄入不足、术前白蛋白<35 g/L是食管癌患者术前存在营养风险的危险因素。术前营养风险较高与术后吻合口瘘发生率升高、住院时间延长有关。提示临床对于食管癌患者术前应积极评估其营养风险，并加强营养支持，以降低术后并发症风险，缩短其住院时间。

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