

doi: 10.3978/j.issn.2095-6959.2018.06.021

View this article at: <http://dx.doi.org/10.3978/j.issn.2095-6959.2018.06.021>

营养预后指数评估术前营养状态对食管癌术后并发症的预测价值

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[摘要] **目的:** 探讨营养预后指数(prognostic nutritional index, PNI)评估术前营养状态对食管癌术后并发症的预测价值。**方法:** 回顾性分析2016年3月至2017年12月154例食管癌行开胸根治术患者的临床资料, 根据PNI划分为低PNI组($PNI < 45$, 中重度营养不良, $n=58$)和高PNI组($PNI \geq 45$, 营养正常或轻度营养不良, $n=96$)。对比2组术后并发症发生情况, 单因素和多因素logistic回归分析影响食管癌术后并发症的相关因素。**结果:** 本组食管癌患者存在营养不良($PNI < 45$)的比例为37.7%(58/154)。低PNI组术后总体并发症(60.3% vs 37.5%)、严重并发症(22.4% vs 10.4%)、手术部位感染(29.3% vs 12.5%)、吻合口瘘(20.7% vs 9.4%)发生率显著高于高PNI组, 差异均具有统计学意义($P < 0.05$)。单因素分析发现年龄、基础疾病、病理分期、术中失血量、新辅助放化疗、手术时间、PNI与术后总体并发症有相关性, 基础疾病、术中失血量、PNI与术后严重并发症有相关性。多因素logistic回归分析发现基础疾病($OR=1.16$, 95%CI 0.987~1.413, $P=0.048$)、低PNI($PNI < 45$)($OR=2.31$, 95%CI 1.058~6.821, $P=0.036$)是术后总体并发症的独立危险因素, 低PNI($PNI < 45$)($OR=2.91$, 95%CI 1.067~10.131, $P=0.040$)是术后严重并发症的独立危险因素。**结论:** 术前低PNI是食管癌开胸根治术后并发症的独立危险因素, 临床上可通过PNI评估术前营养状况, 必要时术前给予营养支持治疗。

[关键词] 营养预后指数; 食管癌; 开胸切除术; 术后并发症; 营养不良

Predictive value of prognostic nutritional index for postoperative complications of esophageal cancer

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Abstract **Objective:** To investigate the predictive value of prognostic nutritional index (PNI) on postoperative complications of esophageal cancer. **Methods:** The clinical data of 154 patients with esophageal cancer underwent thoracotomy and radical resection from March 2016 to December 2017 were retrospectively analyzed and divided into a low-PNI group ($PNI < 45$, moderate to severe malnutrition, $n=58$) and a high-PNI group ($PNI \geq 45$, normal nutrition or light malnutrition, $n=96$). The incidence of postoperative complications between the 2 groups was

收稿日期 (Date of reception): 2018-03-27

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基金项目 (Foundation item): 福建省科技厅军民共建(社发)项目(2016Y5005)。This work was supported by Fujian Provincial Military and Civilian Construction (Social Development) Project of Science and Technology Department, China (2016Y5005).

compared. The factors associated with postoperative complications of esophageal cancer were analyzed by singular and multiple factor logistic regression analysis. **Results:** The proportion of moderate to severe malnutrition (PNI<45) in the series was 37.7% (58/154). In the low-PNI group, the incidence rate of any complications (60.3% vs 37.5%), severe complications (22.4% vs 10.4%), surgical site infection (29.3% vs 12.5%), anastomotic leakage (20.7% vs 9.4%) were significantly higher than those in the high-PNI group ($P<0.05$). Univariate analysis showed that the age, comorbidity, pathological stage, intraoperative blood loss, neoadjuvant chemoradiotherapy, operation time, and PNI were associated with the overall postoperative complications. Moreover, the comorbidity, intraoperative blood loss, and PNI were associated with severe postoperative complications. Multivariate logistic regression analysis showed that the comorbidity (OR=1.16, 95% CI 0.987–1.413, $P=0.048$) and the low PNI (PNI<45) (OR=2.31, 95% CI 1.058–6.821, $P=0.036$) were the independent risk factors of any morbidity, and only the low PNI (PNI<45) (OR=2.91, 95% CI 1.067–10.131, $P=0.040$) was an independent risk factor for severe morbidity. **Conclusion:** Preoperative low PNI index is an independent risk factor for postoperative complications of esophageal cancer underwent thoracotomy and radical resection. The preoperative nutritional status can be assessed by PNI, and preoperative nutritional support should be given if necessary.

Keywords prognostic nutritional index; esophageal cancer; thoracotomy; postoperative complications; malnutrition

食管癌是临床常见的消化道恶性肿瘤之一,患者常表现为吞咽困难、疼痛、出血等症状,长期影响进食可增加营养不良风险^[1]。既往研究^[2]表明:食管癌尤其是老年患者存在营养不良的比例较高,营养不良可导致患者手术风险升高、术后并发症增加、住院时间延长,甚至影响远期生存。目前,评价恶性肿瘤患者术前营养状况的临床指标有体质量指数、近3个月体质量下降幅度、贫血程度和白蛋白水平,其中白蛋白是反映机体短期内营养状况变化的重要指标,术前低蛋白血症与术后并发症发生存在相关^[3]。营养预后指数(prognostic nutritional index, PNI)是通过血清白蛋白和外周血淋巴细胞计数水平换算而成,主要用于胃肠道肿瘤患者营养风险筛查和手术风险评估,但在食管癌手术风险评估、术后并发症预测中的研究较少^[4],尤其缺乏其对术后总体并发症和严重并发症的预测分析。本研究探讨PNI对食管癌开胸根治术患者术后总体并发症和严重并发症的预测价值。

1 资料与方法

1.1 资料

回顾性分析2016年3月至2017年12月解放军福州总医院收治的食管癌行开胸根治术患者154例。纳入标准:1)食管癌病理诊断明确;2)择期行开胸根治术,常规开胸切除、采用统一标准清扫区

域淋巴结,经胸腔打开膈肌,管状胃食管残端重建;3)常规围手术期管理。排除标准:1)急诊手术;2)胸/腹腔镜手术;3)开腹手术;4)胸腹联合手术;5)胃镜下局部切除者;6)姑息性手术;7)病理分期IV期;8)本研究涉及的相关指标缺失者。最终纳入食管癌开胸根治术患者154例,其中男107例、女47例,年龄45~75(65.8 ± 12.4)岁,合并基础疾病78例,术后TNM病理分期:I期6例、II期25例、III期123例。术前接受新辅助放化疗22例、未行新辅助放化疗132例,均接受开胸根治术(管状胃重建),手术时间(175.0 ± 20.5)min,其中<3 h者92例、 ≥ 3 h者62例;术中出血量(400.5 ± 55.2)mL,其中<500 mL者131例、 ≥ 3 h者23例;PNI为 50.4 ± 6.0 ,其中PNI<45者58例、PNI ≥ 45 者96例。

1.2 收集指标

1.2.1 人口学特征

性别和年龄(参照世界卫生组织标准发展中国家尤其是亚太地区以 ≥ 60 岁定义为老年^[5])。

1.2.2 术前指标

1)是否合并基础疾病:慢性阻塞性肺疾病、糖尿病、心血管疾病;2)有无接受新辅助放化疗;3)PNI:查阅术前3 d内血常规和生化检查,采集血清白蛋白(serum albumin, ALB)和淋巴细胞计数(total lymphocyte count, TLC)数据。参照公式计算: $PNI=10\times ALB(g/dL)+0.005\times TLC(mm^{-3})$ ^[6]。

参照国内外统一标准划定PNI截断值为45, 其中PNI<45为中重度营养不良, PNI≥45为营养正常或轻度营养不良^[7]。

1.2.3 术中指标

术中出血量和手术时间。

1.2.4 术后指标

术后并发症情况: 参照文献[8]进行诊断, 1) 肺部并发症。出现以下一项或以上情况: 术后因呼吸衰竭需要初始通气支持超过48 h或再行气管插管, 术后行气管切开术, 并发肺炎(经胸部X线摄片证实术后新发肺部浸润影像, 或支气管肺泡灌洗液培养阳性), 脓胸或乳糜胸, 术后出现的任何需要介入或外科手术干预的肺部疾病。2) 手术部位感染。术后30 d内发生在手术切口、手术深部器官或腔隙的感染。3) 吻合口瘘。出现吻合口瘘的临床征象如经切口和/或引流管流出消化液、食物残渣、脓液, 皮肤红肿, 白细胞计数升高, 体温升高; 和/或经食管造影、胃镜、胸部CT或胸穿证实明确瘘口存在。4) 心血管并发症。心律失常、缺血性心脏病、心力衰竭、心包积液等需要药物或其他干预的心脏并发症, 以及血栓性并发症如肺栓塞、下肢深静脉血栓。5) 参照术后并发症Clavien-Dindo Classification(CDc)分级标准, 总体并发症是指术后任何等级的并发症, 严重并发症是指IIIb级及以上的并发症, 即需要在麻醉状态下进行外科手术、内镜或放射介入干预的并发症^[9]。

TNM病理分期: 参照2017年UICC/AJCC第8版食管癌TNM分期标准^[10]。

1.3 统计学处理

使用SPSS 21.0统计软件进行分析, 计量资料采用均数±标准差($\bar{x} \pm s$)表示, 组间比较采用独立样本t检验; 计数资料采用例数或百分比表示, 组间比较采用卡方检验。进行单因素和多因素logistic回归分析食管癌开胸根治术后并发症的关联因素, 关联性以比值比(OR值)及95%可信区间(95% CI)表示, $P < 0.05$ 为差异具有统计学意义。

2 结果

2.1 低PNI组和高PNI组术后并发症情况比较

本组食管癌患者中, 中重度营养不良(PNI<45)者58例(37.7%); 营养正常或轻度营养不良(PNI≥45)者96例(62.3%)。根据国际统一标准的PNI截断值, 将本组食管癌患者分为低PNI组(PNI<45)和高PNI组(PNI≥45)。低PNI组总体并发症、严重并发症、手术部位感染、吻合口瘘发生率显著高于高PNI组, 差异具有统计学意义($P < 0.05$, 表1)。

2.2 术后总体并发症的单因素和多因素分析

本组食管癌患者术后总体并发症(指任一CDc级的并发症)发生率为46.1%(71/154), 单因素分析发现年龄、基础疾病、病理分期、新辅助放疗、术中出血量、手术时间、PNI均与术后总体并发症存在关联($P < 0.05$)。多因素Logistic回归分析发现, 只有合并基础疾病和低PNI是食管癌术后总体并发症的独立危险因素($P < 0.05$, 表2)。

表1 两组术后并发症情况比较($n=154$)

Table 1 Comparison of postoperative complications between the two groups ($n=154$)

并发症	低PNI组($n=58$)	高PNI组($n=96$)	χ^2	P
总体并发症/[例(%)]			7.594	0.006
有	35 (60.3)	36 (37.5)		
无	23 (39.7)	60 (62.5)		
严重并发症/[例(%)]			4.096	0.043
有	13 (22.4)	10 (10.4)		
无	45 (77.6)	86 (89.6)		
肺部并发症/[例(%)]			3.656	0.056
有	18 (31.0)	17 (17.7)		
无	40 (69.0)	79 (82.3)		
手术部位感染/[例(%)]			6.684	0.010
有	17 (29.3)	12 (12.5)		
无	41 (70.7)	84 (87.5)		

续表1

并发症	低PNI组(n=58)	高PNI组(n=96)	χ^2	P
吻合口瘘/[例(%)]			3.930	0.047
有	12 (20.7)	9 (9.4)		
无	46 (79.3)	87 (90.6)		
吻合口出血/[例(%)]			0.187	0.665
有	4 (6.9)	5 (5.2)		
无	54 (93.1)	91 (94.8)		
吻合口狭窄/[例(%)]			0.576	0.448
有	2 (3.4)	6 (6.2)		
无	56 (96.6)	90 (93.8)		
心血管并发症/[例(%)]			2.273	0.132
有	6 (10.3)	4 (4.2)		
无	52 (89.7)	92 (95.8)		

表2 影响食管癌术后总体并发症的单因素和多因素分析(n=154)

Table 2 Univariate and multivariate analysis of factors affecting postoperative overall complications of esophageal cancer (n=154)

指标	无并发症组(n=83)	并发症组(n=71)	单因素分析		多因素分析	
			t/ χ^2	P	OR (95%CI)	P
性别/[例(%)]			0.343	0.558		
男	56 (67.5)	51 (71.8)				
女	27 (32.5)	20 (28.2)				
年龄/[例(%)]			4.173	0.041	1.13 (0.895~1.347)	0.103
<60	30 (36.1)	15 (21.1)				
≥60	53 (63.9)	56 (78.9)				
合并基础疾病/[例(%)]			5.180	0.023	1.16 (0.987~1.413)	0.048
是	35 (42.2)	43 (60.6)				
否	48 (57.8)	28 (39.4)				
病理分期/[例(%)]			4.552	0.033	2.15 (0.728~4.562)	0.127
I~II	22 (26.5)	9 (12.7)				
III	61 (73.5)	62 (87.3)				
新辅助放化疗/[例(%)]			5.035	0.025	1.24 (0.951~1.386)	0.052
是	10 (12.0)	15 (21.1)				
否	73 (88.0)	56 (78.9)				
术中出血量/[例(%)]			3.975	0.046	1.62 (0.753~3.164)	0.056
<500 mL	75 (90.4)	56 (78.9)				
≥500 mL	8 (9.6)	15 (21.1)				
手术时间/[例(%)]			4.472	0.034	1.47 (0.814~2.165)	0.074
<3 h	56 (67.5)	36 (50.7)				
≥3 h	27 (32.5)	35 (49.3)				
PNI/[例(%)]			5.866	0.015	2.31 (1.058~6.821)	0.036
<45	24 (28.9)	34 (47.9)				
≥45	59 (71.1)	37 (52.1)				

2.3 术后严重并发症的单因素和多因素分析

本组食管癌患者术后严重并发症(指CDc \geq IIIb级的并发症)发生率为14.9%(23/154), 单因素分析发现: 基础疾病、术中出血量、PNI均与术后严重

并发症存在关联($P<0.05$)。多因素Logistic回归分析发现: 只有低PNI是食管癌术后严重并发症的独立危险因素($P<0.05$, 表3)。

表3 影响食管癌术后严重并发症的单因素和多因素分析($n=154$)

Table 3 Univariate and multivariate analysis of factors affecting postoperative severe complications of esophageal cancer ($n=154$)

指标	无严重并发症组($n=131$)	严重并发症组($n=23$)	单因素分析		多因素分析	
			t/χ^2	P	OR (95%CI)	P
性别/[例(%)]			0.251	0.617		
男	90 (68.7)	17 (73.9)				
女	41 (31.3)	6 (26.1)				
年龄/[例(%)]			2.657	0.103		
<60	35 (26.7)	10 (43.5)				
≥ 60	96 (73.3)	13 (56.5)				
合并基础疾病/[例(%)]			3.870	0.049	2.35 (0.628~7.126)	0.104
是	62 (47.3)	16 (69.6)				
否	69 (52.7)	7 (30.4)				
病理分期/[例(%)]			0.126	0.722		
I~II	27 (20.6)	4 (17.4)				
III	104 (79.4)	19 (82.6)				
术中出血量/[例(%)]			5.113	0.024	2.83 (0.845~9.047)	0.052
<500 mL	115 (87.8)	16 (69.6)				
≥ 500 mL	16 (12.2)	7 (30.4)				
手术时间/[例(%)]			1.596	0.207		
<3 h	81 (61.8)	11 (47.8)				
≥ 3 h	50 (38.2)	12 (52.2)				
PNI/[例(%)]			6.202	0.013	2.91 (1.067~10.131)	0.040
<45	44 (33.6)	14 (60.9)				
≥ 45	87 (66.4)	9 (39.1)				

3 讨论

术前营养状况与食管癌围手术期并发症和远期生存密切相关, 营养不良被认为是术后并发症和预后的独立危险因素^[2]。实验室检查中血清白蛋白、转铁蛋白、胆固醇、总淋巴细胞计数等多个指标皆可在一定程度上反映术前营养状况并与术后并发症相关^[11], 但是目前尚缺乏可以更加客观、实用、准确地来预测食管癌术后并发症风险的一个综合指标。

PNI综合了血清白蛋白和总淋巴细胞计数两项指标, 其中血清白蛋白是反映机体蛋白质储备水平的客观营养指标, 低白蛋白血症预示着体内蛋白质被过度消耗; 总淋巴细胞计数也是一项重要的营养和免疫指标, 术前淋巴细胞计数水平较低与术后并发症存在密切相关, 临床研究^[12-13]发现免疫营养制剂通过提高总淋巴细胞计数、增强免疫功能进而可以降低术后并发症。近来, PNI被证实在预测克罗恩病、胃肠道肿瘤术后并发症方面较以往实验室单项指标更具优势, 其

对食管癌术后并发症的预测价值尚缺乏系统性研究^[14-16]。目前,国内外研究基本采用PNI<45为中重度营养不良的评估标准^[17-18]。按照这一划分标准,本研究中食管癌患者术前存在中重度营养不良的比例高达37.7%,但低于杨圣思等^[19]的同类报道,原因在于本组病例以局部进展期食管癌为主,而杨圣思等报道病例以老年晚期食管癌为主,但是本研究结果数据表明局部进展期食管癌患者术前营养不良问题同样较为严峻。本研究通过对低PNI(PNI<45)和高PNI(PNI≥45)患者进行比较发现:低PNI食管癌患者术后总体并发症、严重并发症、手术部位感染、吻合口瘘发生风险均显著升高。单因素分析结果表明PNI与食管癌术后总体并发症和严重并发症的发生均存在一定关联。多因素logistic回归分析发现:低PNI既是术后总体并发症独立危险因素,又是术后严重并发症的独立危险因素。以上结果提示PNI指标不仅对食管癌术后总体并发症具有预测价值,更重要的是还可以作为术后严重并发症的预测指标。术后严重并发症往往需要外科、内镜或介入的有创干预,增加围手术期死亡风险,因此准确预测术后严重并发症将对提前制定防范措施和尽早采取积极有效防治手段具有重要的临床意义^[20-21]。笔者认为:今后应加强对食管癌围手术期营养状况评估,对具有营养风险尤其是营养不良的患者术前给予营养治疗,通过多学科团队制定合理的营养支持治疗方案,术前给予常规营养制剂和免疫营养制剂进行营养干预将有助于改善患者营养和免疫状态,降低食管癌术后并发症风险^[13,22-23]。值得指出的是,本组患者中吻合口瘘的总体发生率为13.6%,尤其是低PNI的患者吻合口瘘的发生率高达20.7%,而高PNI患者吻合口瘘发生率仅9.4%,其中吻合口瘘的总体发生率高于国内外既往报道水平^[24],这主要是由于本组均为老年患者,合并糖尿病等基础疾病比例较高、而且部分患者还接受了术前新辅助放化疗,这些因素是导致本组吻合口瘘发生率较高的主要因素^[25]。另一方面,可能也与本研究中吻合口瘘的诊断病例中既包含了临床显性吻合口瘘,也囊括了影像学发现的隐性吻合口瘘有关。本研究不足之处在于:没有进行各种营养风险筛查工具之间效能的比较,目前在食管癌术后并发症风险预测方面尚缺乏各种营养风险筛查工具之间的对比研究,但是在结直肠癌术后的研究^[26]发现:相较欧洲营养风险筛查工具(Nutritional Risk Screening Tool 2002, NRS 2002)和营养不良通用筛检工具

(Malnutrition Universal Screening Tool, MUST),结直肠癌患者入院时使用营养风险指数(nutrition risk index, NRI)进行营养风险筛查具有更高的效能。

综上所述,本研究结果表明术前低PNI是食管癌术后并发症的独立危险因素,临床上可通过PNI评估术前营养状况,必要时应在术前积极给予营养支持治疗。今后,值得开展包括PNI和NRI在内的各种营养风险筛查工具对食管癌术后并发症预测效能的对比研究。

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本文引用: 李美端, 张娟, 杨胜生, 黄雪玲. 营养预后指数评估术前营养状态对食管癌术后并发症的预测价值[J]. 临床与病理杂志, 2018, 38(6): 1267-1273. doi: 10.3978/j.issn.2095-6959.2018.06.021

Cite this article as: LI Meiduan, ZHANG Juan, YANG Shengsheng, HUANG Xueling. Predictive value of prognostic nutritional index for postoperative complications of esophageal cancer[J]. Journal of Clinical and Pathological Research, 2018, 38(6): 1267-1273. doi: 10.3978/j.issn.2095-6959.2018.06.021