doi:10.11659/jjssx.04E020017

·临床研究·

中性粒细胞—淋巴细胞比预测早期胃癌淋巴结转移的临床价值

王 滔,左芦根,李仕青 (蚌埠医学院第一附属医院胃肠外科,安徽 蚌埠 233000)

[摘 要] **目的** 分析中性粒细胞—淋巴细胞比(NLR)预测早期胃癌(EGC)淋巴结转移的临床价值,以期为 EGC 治疗方案的制订提供参考。**方法** 回顾性分析在我院行胃癌根治术并经术后病理确诊为 EGC 的 134 例患者的临床资料,根据淋巴结是否转移分为阳性组和阴性组。收集 EGC 患者术前 1 周血液学指标并计算血小板—淋巴细胞比(PLR)和 NLR;收集患者基本信息及术后病理信息,行单因素和多因素 *Logistic* 回归分析;通过受试者工作特征(*ROC*)曲线分析 NLR 预测 EGC 伴淋巴结转移阳性的诊断价值;分析术前 NLR 与患者一般资料及临床病理之间的相关性;*Pearson* 相关性检验分析 NLR 与肿瘤大小的相关性;*Kaplan-Meier*(*K-M*)曲线及 *Log-rank* χ^2 检验比较高 NLR 组和低 NLR 组患者术后生存状况。**结果** 单因素分析结果显示,浸润深度、分化程度、肿瘤大小、PLR、NLR 与淋巴结转移相关($P<0.05$)。多因素 *Logistic* 回归分析结果显示,肿瘤大小≥2cm、浸润深度为黏膜下层、分化程度为低分化、NLR≥1.965 是淋巴结转移的独立危险因素($P<0.05$)。根据 *ROC* 曲线,NLR 截断值为 2.295,术前 NLR 预测淋巴结转移的灵敏性和特异性分别为 82.6% 和 77.5%。根据截断值将所有患者分为低 NLR 组(NLR<2.295)90 例和高 NLR 组(NLR≥2.295)44 例,2 组患者一般资料及临床病理相关因素分析结果显示,术前 NLR 与年龄、肿瘤大小、肿瘤大体类型显著相关($P<0.05$)。术前 NLR 与肿瘤大小呈正相关($r=0.645$,$P<0.001$)。术前高 NLR 组患者术后 5 年生存率明显低于低 NLR 组患者($P<0.05$)。**结论** 术前 NLR 对 EGC 患者发生淋巴结转移具有较高的预测价值,且对 EGC 患者预后的评估具有一定的临床参考价值。

[关键词] 早期胃癌;中性粒细胞—淋巴细胞比;淋巴结转移;危险因素;治疗方式

[中图分类号] R446.11 [文献标识码] A [收稿日期] 2020-07-26

Clinical value of neutrophil-lymphocyte ratio in predicting lymph node metastasis of early gastric cancer

WANG Tao, ZUO Lu-gen, LI Shi-qing (Department of Gastrointestinal Surgery, First Affiliated Hospital of Bengbu Medical College, Bengbu Anhui 233000, China)

Abstract: Objective To analyze the clinical value of neutrophil-lymphocyte ratio (NLR) in predicting lymph node metastasis of early gastric cancer (EGC), so as to provide reference for the formulation of treatment plan for EGC. **Methods** The clinical data of 134 patients with EGC diagnosed by pathology after radical gastrectomy in our hospital were retrospectively analyzed, and they were divided into positive

[基金项目] 国家自然科学基金(81702450)

[通信作者] 李仕青,E-mail:LiShiQing8769@sina.cn

[19] Ortiz VE, Vidal-Melo MF, Walsh JL. Strategies for managing oxygenation in obese patients undergoing laparoscopic surgery[J]. Surg Obes Relat Dis, 2015, 11(3): 721-728. doi: 10.1016/j.soard.2014.11.021.

[20] Rudy HL, Cho W, Oster BA, et al. Rapid bodyweight reduction before lumbar fusion surgery increased postoperative complications[J]. Asian Spine J, 2020, 14(5): 613-620. doi: 10.31616/asj.2019.0236.

[21] Li Z, Liu P, Zhang C, et al. Incidence, prevalence, and analysis of risk factors for surgical site infection after lumbar fusion surgery: ≥2-year follow-up retrospective study[J]. World Neurosurg, 2019, 131: e460-e467. doi: 10.1016/j.wneu.2019.07.207.

[22] Jie B, Jiang ZM, Nolan MT, et al. Impact of preoperative nutritional support on clinical outcome in abdominal surgical patients at nutritional risk[J]. Nutrition, 2012, 28(10): 1022-1027. doi: 10.1016/j.nut.2012.01.017.

[23] Liumbruno GM, Bennardello F, Lattanzio A, et al. Recommendations for the use of albumin and immunoglobulins[J]. Blood Transfus, 2009, 7(3): 216-234. doi: 10.2450/2009.0094-09.

[24] Salazar JJ, Ennis WJ, Koh TJ. Diabetes medications: impact on inflammation and wound healing[J]. J Diabetes Complications, 2016, 30(4): 746-752. doi: 10.1016/j.jdiacomp.2015.12.017.

[25] Pennington Z, Lubelski D, Westbroek EM, et al. Persistent postoperative hyperglycemia as a risk factor for operative treatment of deep wound infection after spine surgery[J]. Neurosurgery, 2019, 87(2): 211-219. doi: 10.1093/neuros/nyz405.

[26] Liqing Y, Yuefeng S, Ge L, et al. Is hemoglobin A1c and perioperative hyperglycemia predictive of periprosthetic joint infection following total joint arthroplasty?: A systematic review and meta-analysis[J]. Medicine (Abingdon), 2017, 96(51): e8805. doi: 10.1097/MD.0000000000008805.

[27] Ban KA, Minei JP, Laronga C, et al. Executive summary of the American college of surgeons/surgical infection society surgical site infection guidelines-2016 update[J]. Surg Infect (Larchmt), 2017, 18(4): 379-382. doi: 10.1089/sur.2016.214.

(编辑:龙小芬)

group and negative group according to whether lymph node metastasis was present. Hematological indexes of EGC patients were collected 1 week before surgery, and platelet-to-lymphocyte ratio (PLR) and NLR were calculated. The basic information and postoperative pathological information of patients were collected to conduct univariate analysis and multivariate Logistic regression analysis. The diagnostic value of NLR in predicting positive EGC with lymph node metastasis was analyzed by *receiver operating characteristic* (*ROC*) curve. The correlation between preoperative NLR and patients' general information and clinicopathology was analyzed. *Pearson* correlation test was used to analyze the correlation between NLR and tumor size. *Kaplan-Meier*(*K-M*) curve and *Log-rank* test χ^2 were used to compare the postoperative survival of patients in the high and low NLR groups. **Results** Univariate analysis showed that depth of invasion, degree of differentiation, tumor size, PLR, NLR were correlated with lymph node metastasis ($P<0.05$). Multivariate *Logistic* regression analysis showed that tumor size≥2 cm, depth of invasion(infiltrated into the submucosa), degree of differentiation(poor differentiation) and NLR≥1.965 were the independent risk factors for lymph node metastasis ($P<0.05$). According to the *ROC* curve, the cut-off value of NLR was 2.295, and the sensitivity and specificity of preoperative NLR in predicting lymph node metastasis were 82.6% and 77.5%, respectively. All patients were divided into low NLR group (NLR<2.295, with 90 cases) and the high NLR group (NLR≥2.295, with 44 cases). The analysis results of general data and clinicopathological factors of patients in the two groups showed that the preoperative NLR was significantly correlated with the age, tumor size and general tumor type ($P<0.05$). Preoperative NLR was positively correlated with tumor size ($r=0.645$, $P<0.001$). The 5-year survival rate of patients in the high preoperative NLR group was significantly lower than that of patients in the low NLR group ($P<0.05$). **Conclusion** Preoperative NLR has a certain predictive value for the occurrence of lymph node metastasis in EGC patients, which can provide clinical reference for the prognosis evaluation of EGC patients.

Keywords: early gastric cancer; neutrophil-lymphocyte ratio; lymph node metastasis; risk factors; treatment method

胃癌在消化系统疾病中极为常见,其在日本和我国发生率最高[1],且发病率呈现上升趋势[2]。早期胃癌(early gastric cancer,EGC)是指病灶局限于黏膜层或黏膜下层的胃癌,与有无淋巴结转移及肿瘤大小无关。相比进展期胃癌,EGC 具有更好的预后,5 年生存率大于 90%[3]。然而,既往报道部分 EGC 患者存在淋巴结转移,且淋巴结转移可降低患者 5 年生存率(小于 70%)[4]。因此,明确 EGC 淋巴结转移的危险因素有利于制订综合治疗方案,提高患者预后。日本胃癌治疗指南认为只要怀疑发生淋巴结转移,就应行胃癌根治性手术[5]。目前,EGC 的主要治疗方式包括内镜黏膜下剥离术(endoscopic submucosal dissection,ESD)、内镜下黏膜切除术(endoscopic mucosal resection,EMR)以及胃癌根治术。由于 ESD 创伤较小,恢复较快,长期疗效可与外科手术媲美[6],越来越多的 EGC 患者愿意接受内镜治疗,然而 ESD 的适应证为无淋巴结转移,因此术前预测 EGC 是否伴淋巴结转移对治疗方式的选择具有重要的参考价值[7]。文献回顾显示,肿瘤浸润深度、肿瘤大小等因素可能与 EGC 淋巴结转移相关;此外,血小板—淋巴细胞比(platelet-lymphocyte ratio,PLR)和中性粒细胞—淋巴细胞比(neutrophil-lymphoid ratio,NLR)等炎症指标在多种恶性肿瘤中对淋巴结转移具有预判价值[8-11]。基于以上研究背景,本研究纳入接受胃癌根治术的 EGC 患者,分析影响淋巴结转移的危险因素,以期为此类患者的临床诊疗提供参考。

1 资料与方法

1.1 临床资料

回顾性分析 2011 年 11 月至 2014 年 11 月在我院接受胃癌根治术的 EGC 患者的临床资料。纳入标准:①临床资料完整;②成功接受胃癌根治术(D2 根治术);③术后病理诊断为 EGC。排除标准:①术前接受放化疗;②合并肺癌、肝癌等其他恶性肿瘤;③残胃癌。共计纳入 134 例患者,根据淋巴结是否转移将其分为阳性组($n=23$)和阴性组($n=111$)。阳性组中男 13 例,女 10 例,平均年龄(63.39±9.74)岁;阴性组中男 79 例,女 32 例,平均年龄(57.66±10.51)岁。2 组患者临床资料比较,差异无统计学意义($P>0.05$)。

1.2 方法

1.2.1 单因素分析影响 EGC 淋巴结转移的危险因素

单因素分析纳入指标:①患者一般资料,包括性别、年龄,是否有糖尿病、高血压、心脏病史;②术前 1 周血液学指标,包括白细胞、中性粒细胞、淋巴细胞、癌胚抗原(carcinoembryonic antigen,CEA)浓度(正常参考值为 <5 $ng\cdot mL^{-1}$)[12],计算出 NLR 和 PLR,以中位数将 PLR、NLR 进行二分类数据转换分析;③临床病理资料,包括肿瘤浸润深度、肿瘤大小等。

1.2.2 多因素分析

将单因素分析有统计学差异的指标纳入 *Logistics* 回归模型,分析影响 EGC 患者淋巴结转移的独立风险因素。

1.2.3 NLR 对 EGC 患者淋巴结转移的预判价值及临

床意义 绘制受试者工作特征(*receiver operating characteristic*,*ROC*)曲线,分析 NLR 对 EGC 患者淋巴结转移诊断的预测价值。确定 NLR 的截断值,将小于截断值的患者设为低 NLR 组,大于截断值的患者设为高 NLR 组;分析术前 NLR 与临床病理、肿瘤大小的相关性,及其对 EGC 患者术后 5 年生存率的影响。

1.3 统计学方法

数据分析采用 SPSS 24.0 统计学软件。计量资料以中位数为界限进行二分类转换,计数资料比较采用 χ^2 检验,样本量小于 5 的数据采用 *Fisher* 确切概率检验法,将单因素中 $P<0.05$ 的变量进行多因素 *Logistic* 回归分析,确定独立危险因素。预测诊断价值分析采用 *ROC* 曲线。相关性分析采用 *Pearson* 相关性检验。2 组患者术后生存状况直观比较采用 *Kaplan-Meier*(*K-M*)曲线及 *Log-rank* χ^2 检验。$P<0.05$ 为差异具有统计学意义。

2 结果

2.1 EGC 伴淋巴结转移的单因素分析

单因素分析结果显示:分化程度、浸润深度、肿瘤大小、NLR、PLR 是淋巴结转移的影响因素($P<0.05$)。而性别、年龄、心脏病、糖尿病、高血压、肿瘤溃疡、肿瘤大体类型、肿瘤部位、神经或脉管侵犯、CEA 与淋巴结转移无关($P>0.05$),见表 1。

表 1 影响 EGC 伴淋巴结转移的单因素分析(例)

临床资料		阳性组($n=23$)	阴性组($n=111$)	χ^2	P
性别(男/女)		13/10	79/32	1.900	0.168
年龄(<60 岁/≥60 岁)		8/15	57/54	2.094	0.148
高血压(有/无)		5/18	18/93		0.547
糖尿病(有/无)		1/22	6/105		1.000
心脏病(有/无)		0/23	2/109		1.000
肿瘤溃疡(有/无)		13/10	44/67	2.221	0.136
分化程度(高/低)		12/11	81/30	3.881	0.049
浸润深度(黏膜内/黏膜下)		6/17	65/46	8.064	0.005
肿瘤大小(<2 cm/≥2 cm)		1/22	50/61	13.386	0.000
神经或脉管侵犯(有/无)		1/22	0/111		0.172
CEA(<5 ng·mL^{-1}/≥5 ng·mL^{-1})		19/4	104/7		0.095
NLR(<1.965/≥1.965)		2/21	65/46	18.948	0.000
PLR(<135.150/≥135.150)		3/20	64/47	15.169	0.000
肿瘤大体类型	凹陷型	7	50	1.988	0.370
	平坦型	8	26		
	隆起型	8	35		
肿瘤部位	胃窦	13	60	2.215	0.529
	胃体	3	17		
	胃角	2	20		
	贲门	5	14		

2.2 EGC 伴淋巴结转移的多因素分析

将单因素分析所得阳性结果纳入 *Logistic* 回归模型,结果发现肿瘤大小≥2 cm、浸润深度为黏膜下层、分化程度为低分化、NLR≥1.965 是发生淋巴结转移的独立危险因素($P<0.05$),见表 2。

表 2 影响 EGC 伴淋巴结转移的多因素分析

变量	*B*	*S.E*	*Wald*	*P*	*OR*	95% *CI*
肿瘤大小(≥2 cm)	2.182	1.104	3.907	0.048	8.864	1.018~77.152
分化程度(低分化)	2.126	0.680	9.774	0.002	8.384	2.211~31.800
浸润深度(黏膜下层)	1.561	0.645	5.858	0.016	4.765	1.346~16.872
NLR(≥1.965)	1.411	0.470	9.003	0.003	4.101	1.631~10.308
PLR(≥135.150)	0.003	0.004	0.370	0.543	0.997	0.989~1.006

2.3 术前 NLR 判断 EGC 淋巴结转移阳性的诊断价值分析

根据 *ROC* 曲线,NLR 截断值为 2.295,术前 NLR 预测淋巴结转移的灵敏性和特异性分别为 82.6% 和 77.5%,曲线下面积为 0.826,95% *CI* 为 0.738~0.915,见图 1。

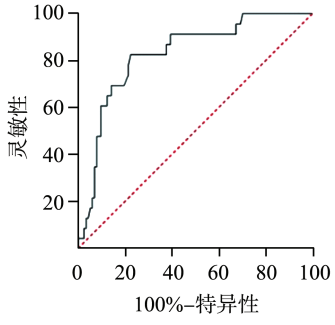


图 1 NLR 对淋巴结转移的预测 *ROC* 曲线图

2.4 术前 NLR 与患者一般资料及临床病理关系

根据 NLR 截断值 2.295,将所有患者分成低 NLR 组(NLR<2.295)90 例和高 NLR 组(NLR≥2.295)44 例,2 组患者一般资料及临床病理相关因素分析结果显示,术前 NLR 与肿瘤大小、肿瘤大体类型以及年龄有关($P<0.05$),与性别、高血压、糖尿病、心脏病、肿瘤溃疡、浸润深度、肿瘤部位、分化程度、神经或脉管侵犯、CEA 无相关性($P>0.05$),见表 3。

2.5 术前 NLR 与肿瘤大小的相关性分析

术前 NLR 与肿瘤大小呈显著正相关($r=0.645$,$P<0.05$),见图 2。

2.6 术前 NLR 对 EGC 患者术后 5 年生存率的影响

本研究纳入的 EGC 患者 5 年生存率为 90.3%(121/134),术前低 NLR 组 EGC 患者 5 年生存率为 94.4%(85/90),高 NLR 组 EGC 患者 5 年生存率为 81.8%(36/44),术前低 NLR 患者 5 年生存率明显优于高 NLR 组(*Log-rank* $\chi^2=5.466$,$P<0.05$),见图 3。

表3 NLR与患者一般资料及临床病理关系(例)

临床资料		低NLR组(n=90)	高NLR组(n=44)	χ^2	P
性别(男/女)		63/27	29/15	0.230	0.632
年龄(<60岁/≥60岁)		51/39	14/30	7.305	0.007
高血压(有/无)		18/72	5/39	1.550	0.213
糖尿病(有/无)		3/87	4/40		0.217
心脏病(有/无)		2/88	0/44		1.000
肿瘤溃疡(有/无)		40/50	17/27	0.408	0.523
分化程度(高/低)		58/32	35/9	3.174	0.075
浸润深度(黏膜内/黏膜下)		53/37	18/26	3.835	0.050
肿瘤大小(<2 cm/≥2 cm)		45/45	6/38	16.576	0.000
神经或脉管侵犯(有/无)		0/90	1/43		0.328
CEA(<5 ng·mL^{-1}/≥5 ng·mL^{-1})		85/5	38/6		0.176
肿瘤大体类型	凹陷型	45	12	6.249	0.044
	平坦型	20	14		
	隆起型	25	18		
肿瘤部位	胃窦	50	23	7.271	0.064
	胃体	16	4		
	胃角	16	6		
	贲门	8	11		

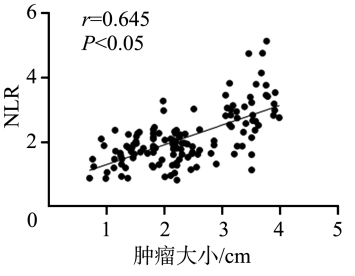


图2 术前NLR与肿瘤大小相关性分析

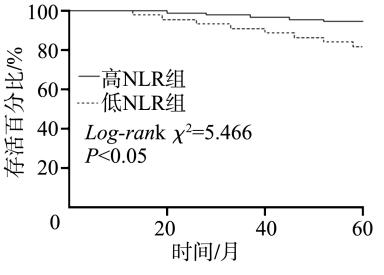


图3 术前高NLR与低NLR对EGC患者生存率的影响

3 讨论

随着我国医疗水平的进步和人民健康意识的提高,相当一部分胃癌患者得以在早期获得明确诊断[13-14]。随着微创理念不断深入,近年来ESD、EMR等内镜技术在EGC的治疗中取得了较好疗效。相比于胃癌根治术,ESD、EMR等内镜下手术具有更小的创伤及更短的康复周期。有研究显示,内镜下治疗EGC具有风险较低、住院时间较短、术后并发症低等优势[15]。但内镜治疗EGC的适应证是无淋巴结转移,即便是早期肿瘤,如存在淋巴结转移则需要行胃癌根治术[16]。因此,判断有无淋巴结转移对于EGC治疗方式的选择具有重要意义。本研究以此为切入点,分析影响EGC患者发生淋巴结转移的危险因素,并重点分析NLR对于EGC发生淋巴结转移的预测价值。

在本研究结果显示,浸润深度达黏膜下层的EGC发生淋巴结转移的风险高于黏膜内EGC,与Kim等[17]的研究结果一致,可能是因为黏膜下层淋巴组织更丰富。既往有研究表明,EGC伴淋巴结转移与神经或脉管侵犯相关[18],而本研究结果则显示,神经或脉管侵犯与淋巴结转移无关,可能是由于本研究样本量较少,待扩大样本量进一步研究。EGC肿瘤越大伴发淋巴结转移的风险越高,这与Gu等[19]的研究结果一致,分析原因可能是肿瘤越大,肿瘤内部组织结构发生改变的可能性越大,增加了淋巴结转移的风险。低分化的EGC患者具有高淋巴结转移风险,这与Guo等[20]的研究结果相符,可能是由于分化程度越低的肿瘤细胞核染色质越丰富,增加了癌细胞转移和侵袭的能力。以上研究结果表明肿瘤浸润深度、肿瘤大小及病理类型是影响EGC患者淋巴结转移的独立危险因素,可为EGC患者手术方案的制订提供参考。

本研究还发现,NLR是EGC伴淋巴结转移的独立危险因素,提示高NLR具有高淋巴结转移风险,与Kosuga等[21]得出的NLR可以预测胃癌淋巴结转移的结论相符。中性粒细胞可通过释放生长因子和趋化因子,促进癌细胞的生长和转移[22],而淋巴细胞是人体免疫系统重要组成成分,可以攻击癌细胞从而发挥抑制癌细胞生长的作用,淋巴细胞的下调会加速癌细胞的增殖、分化[23]。有研究证明,PLR在预测EGC伴淋巴结转移方面具有诊断价值,而NLR不能预测淋巴结转移[24-25],本研究结果与之不一致,可能是由于免疫和炎症早期致瘤事件影响目前还不明确。因此,NLR对EGC患者淋巴结转移发生的预判价值仍然需要更大样本的前瞻性研究予以证实。本研究还发现,术前NLR与年龄、肿瘤大小、肿瘤大体类型相关,且NLR与肿瘤大小呈显著正相关,提示NLR与肿瘤进展存在一定联系。此外,本研究纳入的EGC患者5年生存率大于90%,采用*K-M*生存分析表明,低NLR组患者整体生存状况优于高NLR组,提示术前NLR的表达水平可以在一定程度上预测EGC患者的预后,这与Miyatani等[26]的研究结果相符。

本研究认为对于EGC患者,术前准确预测有无淋巴结转移,有助于制订更为合理的诊疗方案,从而提高综合治疗效果;NLR作为一种简单且易得的炎症指标,可以结合EGC患者淋巴结转移的高危因素来预测EGC患者是否伴有淋巴结转移,临床实用性较强。虽然本研究得出NLR可作为EGC伴淋巴结转移预测指

标的结论,但由于样本量较少且为单中心研究,尚需大样本、多中心的研究数据进一步证实。

综上,NLR、肿瘤大小、分化程度、浸润深度是 EGC 患者伴淋巴结转移的独立风险因素;NLR 和肿瘤大小及肿瘤进展密切相关,对是否伴有淋巴结转移具有一定辅助诊断价值,以及对 EGC 患者预后的评估具有一定的临床参考价值。

[参考文献]

[1] Ferlay J, Colombet M, Soerjomataram I, et al. Estimating the global cancer incidence and mortality in 2018: GLOBOCAN sources and methods [J]. Int J Cancer, 2019, 144(8): 1941 – 1953. doi: 10.1002/ijc.31937.

[2] Bray F, Ferlay J, Soerjomataram I, et al. Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries[J]. CA Cancer J Clin, 2018, 68(6): 394 – 424. doi: 10.3322/caac.21492.

[3] Feng Q, May MT, Ingle S, et al. Prognostic models for predicting overall survival in patients with primary gastric cancer: a systematic review[J]. Biomed Res Int, 2019: 5634598. doi: 10.1155/2019/5634598.

[4] Lee IS, Kang HJ, Park YS, et al. Prognostic impact of extranodal extension in stage 1B gastric carcinomas[J]. Surg Oncol, 2018, 27(2): 299 – 305. doi: 10.1016/j.suronc.2018.05.014.

[5] Japanese Gastric Cancer Association. Japanese gastric cancer treatment guidelines 2014 (ver. 4)[J]. Gastric Cancer, 2017, 20(1): 1 – 19. doi: 10.1007/s10120 – 016 – 0622 – 4.

[6] Cho JH, Cha SW, Kim HG, et al. Long-term outcomes of endoscopic submucosal dissection for early gastric cancer: a comparison study to surgery using propensity score-matched analysis [J]. Surg Endosc, 2016, 30(9): 3762 – 3773. doi: 10.1007/s00464 – 015 – 4672 – 1.

[7] Nishizawa T, Yahagi N. Long-term outcomes of using endoscopic submucosal dissection to treat early gastric cancer [J]. Gut Liver, 2018, 12(2): 119 – 124. doi: 10.5009/gnl17095.

[8] Catal O, Ozer B, Sit M. Prediction of lymph node metastasis in colon cancer via platelet to lymphocyte ratio and platelet count [J]. J Coll Physicians Surg Pak, 2020, 30(3): 250 – 253. doi: 10.29271/jcpsp.2020.03.250.

[9] Aoyama T, Takano M, Miyamoto M, et al. Pretreatment neutrophil-to-lymphocyte ratio was a predictor of lymph node metastasis in endometrial cancer patients[J]. Oncology, 2019, 96(5): 259 – 267. doi: 10.1159/000497184.

[10] Tao L, Zhang LF, Peng Y, et al. Preoperative neutrophil-to-lymphocyte ratio and tumor-related factors to predict lymph node metastasis in patients with pancreatic ductal adenocarcinoma (PDAC)[J]. Oncotarget, 2016, 7(45): 74314 – 74324. doi: 10.18632/oncotarget.11031.

[11] Acharya S, Rai P, Hallikeri K, et al. Preoperative platelet lymphocyte ratio is superior to neutrophil lymphocyte ratio to be used as predictive marker for lymph node metastasis in oral squamous cell carcinoma[J]. J Investig Clin Dent, 2017, 8(3): 1 – 8. doi: 10.1111/jicd.12219.

[12] Lazr DC, Avram MF, Romoşan I, et al. Prognostic significance of tumor immune microenvironment and immunotherapy: novel insights and future perspectives in gastric cancer[J]. World J Gastroenterol, 2018, 24(32): 3583 – 3616. doi: 10.3748/wjg.v24.i32.3583.

[13] Zhao LY, Yin Y, Li X, et al. A nomogram composed of clinicopathologic features and preoperative serum tumor markers to predict lymph node metastasis in early gastric cancer patients[J]. Oncotarget, 2016, 7(37): 59630 – 59639. doi: 10.18632/oncotarget.10732.

[14] Chen W, Zheng R, Baade PD, et al. Cancer statistics in China, 2015[J]. CA Cancer J Clin, 2016, 66(2): 115 – 132. doi: 10.3322/caac.21338.

[15] Liang XQ, Wang Z, Li HT, et al. Indication for endoscopic treatment based on the risk of lymph nodemetastasis in patients with undifferentiated early gastric cancer[J]. Asian J Surg, 2020, 43(10): 973 – 977. doi: 10.1016/j.asjsur.2019.12.002.

[16] Hatta W, Gotoda T, Oyama T, et al. Correction: a scoring system to stratify curability after endoscopic submucosal dissection for early gastric cancer: "eCura system"[J]. Am J Gastroenterol, 2019, 114(12): 1925 – 1926. doi: 10.14309/ajg.0000000000000432.

[17] Kim SM, Lee H, Min BH, et al. A prediction model for lymph node metastasis in early-stage gastric cancer: toward tailored lymphadenectomy[J]. J Surg Oncol, 2019, 120(4): 670 – 675. doi: 10.1002/jso.25628.

[18] Kim Yi, Lee JH, Kook MC, et al. Lymph node metastasis risk according to the depth of invasion in early gastric cancers confined to the mucosal layer[J]. Gastric Cancer, 2016, 19(3): 860 – 868. doi: 10.1007/s10120 – 015 – 0535 – 7.

[19] Gu LH, Chen M, Khadaroo PA, et al. A risk-scoring model for predicting lymph node metastasis in early gastric cancer patients: a retrospective study and external validation[J]. Gastrointest Surg, 2018, 22(9): 1508 – 1515. doi: 10.1007/s11605 – 018 – 3816 – 8.

[20] Guo CG, Zhao DB, Liu Q, et al. A nomogram to predict lymph node metastasis in patients with early gastric cancer[J]. Oncotarget, 2017, 8(7): 12203 – 12210. doi: 10.18632/oncotarget.14660.

[21] Kosuga T, Konishi T, Kubota T, et al. Clinical significance of neutrophil-to-lymphocyte ratio as a predictor of lymph node metastasis in gastric cancer[J]. BMC Cancer, 2019, 19(1): 1187. doi: 10.1186/s12885 – 019 – 6404 – 8.

[22] Liang W, Ferrara N. The complex role of neutrophils in tumor angiogenesis and metastasis[J]. Cancer Immunol Res, 2016, 4(2): 83 – 91. doi: 10.1158/2326 – 6066.CIR – 15 – 0313.

[23] Ogiya R, Niikura N, Kumaki N, et al. Comparison of tumor-infiltrating lymphocytes between primary and metastatic tumors in breast cancer patients[J]. Cancer Sci, 2016, 107(12): 1730 – 1735. doi: 10.1111/cas.13101.

[24] Lou N, Zhang L, Chen XD, et al. A novel scoring system associating with preoperative platelet/lymphocyte and clinicopathologic features to predict lymph node metastasis in early gastric cancer[J]. J Surg Res, 2017, 20(9): 153 – 161. doi: 10.1016/j.jss.2016.10.011.

[25] Zhu GS, Tian SB, Wang H, et al. Preoperative neutrophil lymphocyte ratio and platelet lymphocyte ratio cannot predict lymph node metastasis and prognosis in patients with early gastric cancer: a single institution investigation in China[J]. Curr Med Sci, 2018, 38(1): 78 – 84. doi: 10.1007/s11596 – 018 – 1849 – 6.

[26] Miyatani K, Saito H, Kono Y, et al. Combined analysis of the pre-and postoperative neutrophil-lymphocyte ratio predicts the outcomes of patients with gastric cancer[J]. Surg Today, 2018, 48(3): 300 – 307. doi: 10.1007/s00595 – 017 – 1587 – 6.

(编辑:刘 艺)